EPIDEMIOLOGICAL PROFILE, CLINICO-PATHOLOGICAL CORRELATION AND TREATMENT RESPONSE IN ADULT PATIENTS WITH PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS

Dissertation submitted to

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for the award of the degree of

DM (NEPHROLOGY) – BRANCH – III

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DECLARATION

I solemnly declare that this dissertation titled “Epidemiological profile ,clinico-pathological correlation and treatment response in adult patients with primary focal segmental glomerulosclerosis” is done by me in the Department of Nephrology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance and supervision of Prof.N.Gopalakrishnan, MD., DM., FRCP., Professor & Head of the Department, Department of Nephrology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of the degree of D.M.Nephrology.

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CERTIFICATE

This is to certify that the Dissertation entitled, **"Epidemiological profile ,clinico-pathological correlation and treatment response in adult patients with primary focal segmental glomerulosclerosis"** is the bonafide record work done by Dr.J.Dhanapriya, under our guidance and supervision in the Department of Nephrology, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai, submitted as partial fulfillment for the requirements of D.M. Degree examination Branch III NEPHROLOGY, AUGUST 2013, under Dr.M.G.R. Medical University, Chennai.

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CONTENTS

INTRODUCTION

Focal segmental glomerulosclerosis (FSGS) is a common cause of nephrotic syndrome, accounting for 10% to 35% of nephrotic syndrome in adults [1]. Focal segmental glomerulosclerosis is a pattern of injury defined by a segmental scar, that involves some but not all glomeruli. The prognosis of FSGS in untreated patients is poor , with 50% patients reach end-stage renal disease (ESRD) at eight years. FSGS account for 20% of dialysis patients and is a common cause of ESRD. The incidence of FSGS has been increasing in recent years. Kitiyakara et al. reported an 11-fold increase in FSGS among dialysis patients older than 21 years [2] . Treatment with steroids for 1-2 months has minimal effect on outcomes. Studies have shown that , high-dose glucocorticoids for longer periods of more than five months improved remission rate from 15% to 50% [3] . Patients with primary FSGS treated with prednisolone , are more likely to enter remission than untreated one. Remission rates of 80% can be achieved with longer treatment, and is an independent predictor of renal survival [4]. Five pathologic variants of idiopathic focal segmental glomerulosclerosis [5] : collapsing , cellular , tip lesion , perihilar, and not otherwise specified . Not Otherwise Specified is the most common histo-pathological subtype reported in most of the series.

In adults, responsiveness to steroids usually take up to 16 weeks, and can be slowly tapered over three to six months. Therapy for steroid-resistant FSGS is calcineurin inhibitor, either cyclosporine or tacrolimus. Patients who have persistent proteinuria are also at high risk of cardiovascular morbidity and mortality. FSGS can be broadly classified into primary , secondary , syndromic , and familial [6].

AIM AND OBJECTIVES

1. To study the epidemiological profile of primary focal segmental glomerulosclerosis in adults.
2. To study the clinicopathologic correlation and prevalence of subtypes of FSGS , according to Columbia classification.
3. To evaluate the response to treatment, predictors of poor response and risk factors in the progression to chronic kidney disease in these patients.

REVIEW OF LITERATURE

1.DEFINITION

Focal segmental glomerulosclerosis is defined as segmental increase in mesangial matrix with obliteration of the capillaries, sclerosis, hyalinosis, foam cells, and segmental scarring , and adhesion between the glomerular tuft and Bowman's capsule involving less than 50% of glomerulus and affecting less than 50% of glomeruli [7] . This is characterized by marked proteinuria, steroid resistance, hypertension, and a higher progression[8] to chronic kidney disease (CKD). The diagnosis of primary FSGS is usually made with typical lesion involving some of the glomeruli with others remaining uninvolved in the renal biopsy, with no clinical or pathological evidence of disease that might produce secondary FSGS.

2. INCIDENCE

The incidence of FSGS among children with nephrotic syndrome was 10% in less than six years, reaches upto 20–50% in the adolescence. It accounts for 20 - 25% of idiopathic nephrotic syndrome in adults [9] . Recent reports reveal upto an eightfold raise in the incidence of FSGS in the past two decades. An observational study showed that FSGS was found in 2.5–4% of renal biopsies in 1970s and increased to 12.2–18.7% in 1990s [10] . FSGS is becoming the commonest disease in native kidney biopsies and is the most common primary glomerular disease causing ESRD in the United States [11] and its prevalence was 4%.

3.HISTORY

Theodor Fahr was the first to describe FSGS in 1925 in adult nephrotic patients [12]. However , Arnold Rich [13] was the one who clearly defined the histological lesion in nephrotic children in 1957. Later Jack Churg, Rene Habib and Richard, pathologists of International Study of Kidney Disease in Children , reported the presence of this type of lesion in renal biopsies taken from 1966 to 1969 in childhood nephrotics [14,15].

4.CLASSIFICATION

Classification of FSGS include primary , genetic and secondary. Primary (Idiopathic) occurs without known inciting injury [16]. Secondary FSGS occurs in association with human immunodeficiency virus (HIV) infection [17] , parvovirus, cytomegalovirus, drug toxicity (pamidronate, interferon, lithium, anabolic steroids) , malignancies and heroin nephrotoxicity and immune complex diseases. The commonest type of secondary FSGS is included under adaptive or hyperfiltering FSGS. Alteration in glomerular hemodynamics, resulting in afferent arteriolar vasodilation and increased intracapillary hydrostatic pressure is the cause behind these types of FSGS.

Adaptive FSGS include

Conditions with reduced renal mass: oligomeganephronia, , unilateral renal agenesis, renal dysplasia, reflux nephropathy, low birth weight, surgical renal ablation, aging kidney ,renal allograft.

Conditions with normal renal mass: systemic hypertension, acute or chronic vaso-occlusive processes (thrombotic microangiopathy, renal-artery stenosis, atheroembolization) , sickle cell anemia , obesity,cyanotic congenital heart disease. Obesity-related FSGS is currently the most frequent type of secondary FSGS [18,19].

Genetic causes include defects affecting the expression and function of proteins podocin (NPHS2) , nephrin, alpha-actinin-4, TRPC6, CD2AP, synaptopodin that present in slit diaphragm and podocyte [20] . Early onset of disease and a family history of nephrotic syndrome should arise the suspicion of genetic FSGS. Nephrin (*NPHS1*) was first cloned in congenital nephrotic syndrome of the Finnish type [21] .

The NPHS1 gene is present on chromosome 19q13 and encodes for Nephrin. The protein nephrin is a 185 kDa protein with an intracellular, single transmembrane and extracellular domain. Subsequently, additional genes [22] including podocin, alpha-actinin-4 (ACTN4/FSGS1),transient receptor potential cation channel, type 6 (TRPC6/FSGS2), CD2- associated protein (CD2AP/FSGS3) and phospholipase c E1 (PLCE1/NPHS3) as causes for hereditary nephrotic syndromes (FSGS) [23,24] have been identified. Podocin mutations are responsible for the autosomal recessive (AR) form of steroid-resistant nephrotic syndrome. Podocin is a 42-kD transmembrane protein

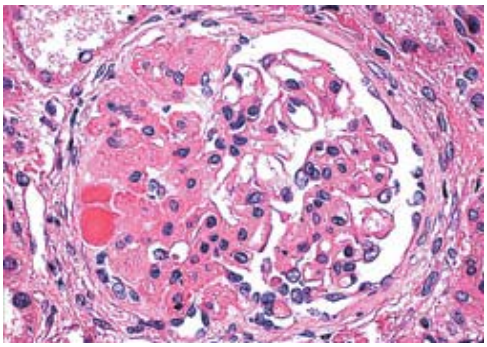
present in podocytes that consists of a short extracellular domain followed by a transmembrane-spanning region and a long cytoplasmic tail.

5.PATHOLOGY

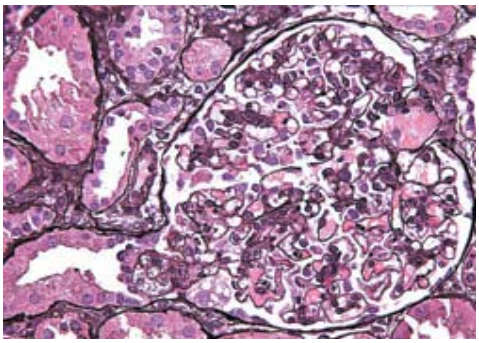
The confirmation of FSGS is essentially done by renal biopsy .Light microscopy shows focal and segmental solidification of the glomerular tuft, adhesion of the tuft to the Bowman capsule (synechiae) , hyalinosis, intraglomerular foam cells ,hypertrophy of podocytes, bridging of parietal cells, focal interstitial fibrosis and tubular atrophy and minimal inflammation, restricted to the areas of fibrosis [25] . On immunofluorescence, there is focal and segmental staining of immunoglobulin M, C3, and occasionally C1q in the areas of sclerosis and hyalinosis. Staining for albumin may be found within the podocytes, corresponding to intracytoplasmic protein resorption droplets.

In electron microscopy, the lesions of segmental sclerosis show wrinkling and retraction of glomerular basement membrane (GBM) and accumulation of hyaline within the membrane, resulting in occlusion of the glomerular capillary lumina [26] . Hyaline deposits contain membranous particles or electron lucent lipid globules. Intraglomerular foam cell appears as large intracapillary cell that contain electron lucent vacuoles .Variable degree of foot process effacement is seen directly overlying the lesions of segmental sclerosis. Focal aggregation of the actin filaments against the abluminal surface of podocytes

accompanied by podocyte hypertrophy, increased organellar content will also be seen. Focal microvillous transformation is due to the formation of thin cellular projections that resemble villi along the surface of podocytes . Hypertrophied podocytes may adhere smoothly to or focally detached from GBM with interposition of newly formed extracellular matrix.



FSGS NOS



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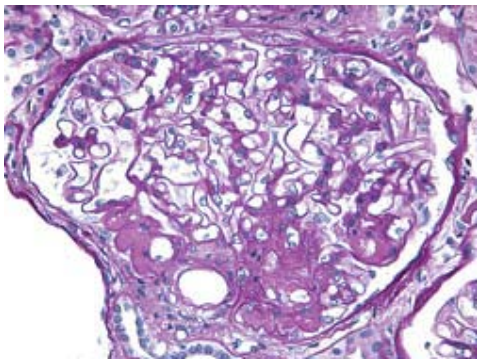

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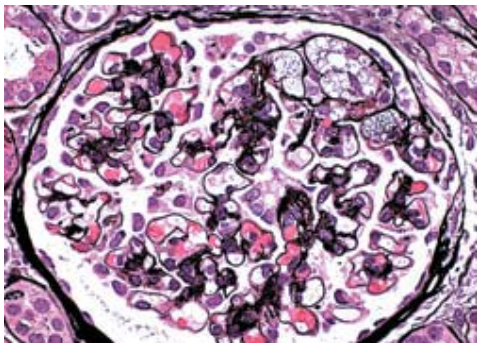
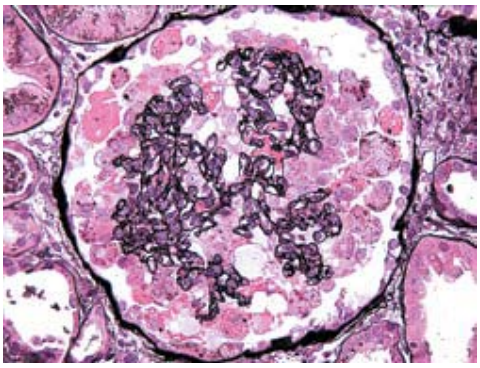


CELLULAR



COLLAPSING FSGS

A working group has defined five subtypes of focal segmental glomerulosclerosis [27] based on light microscopic assessment (Columbia classification) which include

Collapsing FSGS - this is defined as collapse of at least one capillary loop accompanied by obliteration of the lumen with hyperplasia and hypertrophy of the overlying podocytes , regardless of the presence or absence of other lesions. In contrast to original description,working classification does not include tubulointerstitial changes for the diagnosis of this variant.

Tip lesion – This variant is diagnosed by exclusion of collapsing FSGS with at least one glomerulus with segmental lesion involving the tip of the glomerular capillary . A segmental lesion is defined as the presence of endocapillary hypercellularity (involving < 50% of the tuft), or sclerosis (of < 25% of the glomerlar tuft) and foam cells. The tip domain is defined as the outer 25% of the glomerulus next to proximal tubular origin.

Cellular Variant – For diagnosis of this type the exclusion of collapsing and tip variant of FSGS is necessary. It is defined by the presence of at least one glomerulus with segmental endocapillary proliferation occluding the lumina [28,29] .This may be accompanied with or without karyorrhexis .

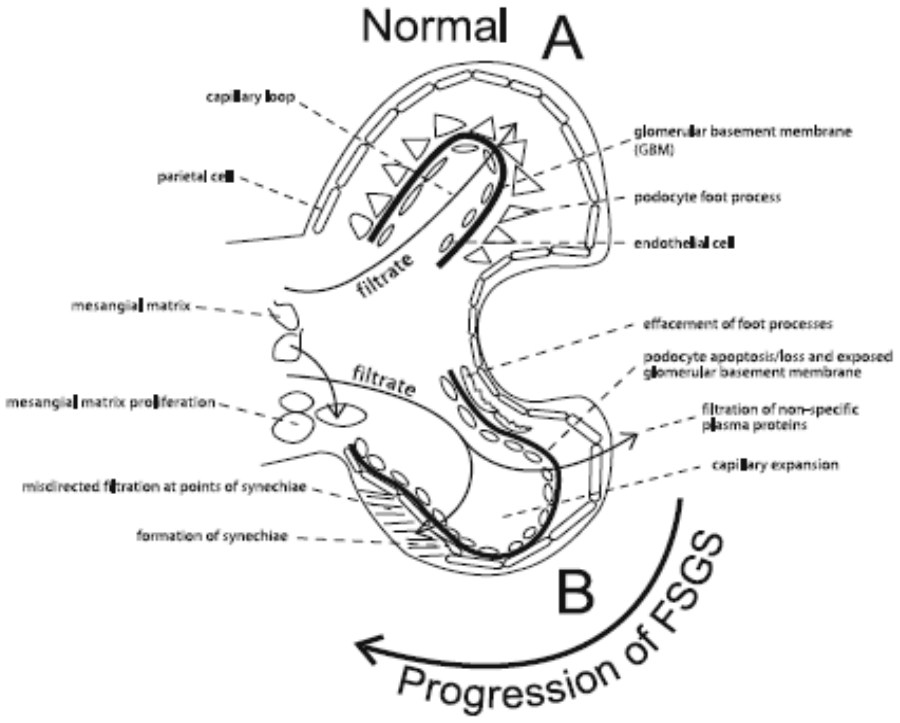
Perihilar variant – this is defined as the segmental sclerotic lesion with or without hyalinosis at the vascular pole usually opposite to the tubular pole .

Presence of all other lesions like tip, cellular or collapsing within the same biopsy should be excluded before making a diagnosis of this variant.

Not Otherwise Specified or NOS is diagnosed when all other lesions by definitions are excluded. Segmental solidification of the glomerular tuft in any portion of the glomerulus usually accompanied by adhesion of the tuft to the Bowman's capsule is seen in this variant.

6.PATHOPHYSIOLOGY

The key pathogenesis of FSGS is podocyte damage and loss. Injury to podocytes occurs by four mechanisms : alteration of the slit diaphragm or interference with its structure, dysregulation of the actin based cytoskeleton, alteration of the GBM or its interactions with the podocyte, or alteration of the negative charge of the podocyte surface. These progressive changes lead to foot process effacement and apoptosis of podocyte, formation of synechiae, filtration of non-specific plasma proteins, misdirected filtration at points of synechiae, capillary expansion and mesangial matrix expansion [30,31] .These summary of events are given below.



Cytokines and vasoactive substances also play a role in the progression of FSGS. In animal model, overexpression of transforming growth factor β and its effector proteins , Smads lead to glomerulosclerosis. Cytokines lead to recruitment of monocytes, macrophages, and T-cells. This inturn stimulates interleukin-1, tumor necrosis factor alpha, and chemokines . Platelet derived growth factor and vascular endothelial growth factor also play a role in the progression of disease. The inflammatory infiltrate leads to mesangial matrix deposition, promoting the collapse of glomeruli. Cellular infiltrates and cytokines damage tubular epithelial cells, and these cells may undergo transformation to mesenchymal cells (called as epithelial-mesenchymal transition or EMT) . The presence of plasma proteins in the glomerular filtrate also causes direct injury to the tubulointerstitium. The mesenchymal cells and the recruited , stimulated fibroblasts, cause matrix deposition and tubulointerstitial fibrosis[31,32] .

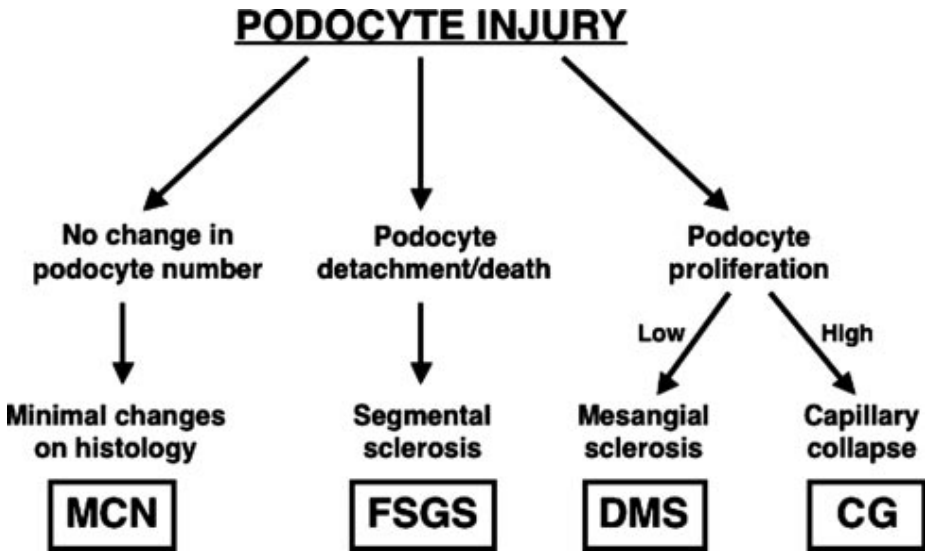
Two genes, MYH9 that encodes myosin heavy chain 9 which is a component of podocyte and APOL1 were identified on chromosome 22 and its role related to FSGS were described recently [33,34] . *APOL1* with G1 and G2 variants was identified as the susceptibility gene and act on podocyte mechanistically (seen commonly in Africo-Americans) to cause FSGS [35] .

Cardiotrophin-like cytokine 1 is a member of interleukin-6 family with a molecular weight of < 30 kDa . CLC1 and soluble urokinase receptor (SUPAR) are implicated in patogenesis of FSGS [36] .Circulating SUPAR induces foot process effacement by activating β3 integrin in podocyte . Serum levels of more than 3000 pg /ml were documented in two thirds of patients with idiopathic FSGS but not in minimal change disease [37] .

Still there is a debate whether FSGS and minimal change disease (MCD) is continuum of single entity or different diseases.The support to the identity of the two diseases is the repeated description of some patients with initially steroid-sensitive disease and minimal change on histology, who evolve to FSGS and develop corticosteroid resistance, end-stage renal disease and sometimes recurrent disease. Intense immunosuppression can on occasion cause remission in patients with renal impairment and FSGS [38] . But more recent advances show difference in pathogenesis of both the entity with involvement of circulating factors in the pathogenesis of FSGS and early recurrence of FSGS after renal transplantation.An essential difference between these two entities is

that rearrangement of actin cytoskeleton, typically reverse with steroid therapy in MCD but irreversible and progressive in FSGS.

Recently FSGS is included under umbrella term 'podocytopathy' with common pathophysiologic principle of absolute or relative podocyte depletion and injury [39] .



7.ANIMAL MODEL

Animal model of FSGS include BALB/c mice with doxorubicin induced lesions [40] and Th Buffalo/mna rats . Another one is the mouse model with puromycin aminonucleoside nephrosis.In vitro studies showed enhanced permeability of glomerulus to albumin and transient proteinuria when serum

from FSGS patients were injected into Sprague-Dawley rats [41,42] . This confirms the presence and implication of circulating factors in the pathogenesis of FSGS.

8.CLINICAL PRESENTATION

Nephrotic syndrome is usually present in 60% at onset and may increase upto 80–90% with time [43] . Secondary FSGS rarely present with a full nephrotic syndrome, and typically slower in onset , with less proteinuria , preserved serum albumin ,and less edema. In primary FSGS, macroscopic haematuria is very rare, but usually associated with micro-hematuria (50%), hypertension (60%), and decreased kidney function (25%-50%) [44] . Proteinuria in FSGS is predominanty nonselective compared to selective proteinuria in MCD [45] .

9.CLINICOPATHOLOGICAL CORRELATION

Schwartz and Lewis [29] in 1985, recognized that patients with the cellular lesion were more often present with nephrotic syndrome than classic FSGS patients . Howie *et al.* found that patients with tip lesion [46] experienced 48% remission with prednisolone , and 10-yr renal survival rate of 90% . However, in the remaining non-remitters (52%) , the 10-yr renal survival was 30%. Stokes *et al.* showed that the presentation , course and outcome in tip variant

was similar to MCD [28] .Remission was highest for tip variant, intermediate for NOS variants, cellular and perihilar and least for collapsing FSGS.

10.TREATMENT

Immunosuppressive agents are the mainstay of treatment in primary FSGS which include steroids, calcineurin inhibitors, cytotoxics whereas a conservative approach is recommended in genetically-determined FSGS as immunosuppressants are not usually effective in these group [47] .

The main aim of therapy is the induction of remission of proteinuria either complete or partial with better preservation of kidney function. Even achievement of partial remission improves the long-term renal survival. Steroid therapy is the first line of therapy unless the side effects of glucocorticoid therapy like diabetes, psychiatric disorder, or severe osteoporosis, where calcineurin inhibitor will be the initial choice of treatment .

Treatment of primary FSGS in adults must be graded according to the presence or absence of factors affecting prognosis adversely . One meta-analysis revealed CR in 61% who were treated for longer periods with prednisolone , whereas it was 15% in those with shorter duration (< 4 months). Most of the patients attained remission after six months. Higher remission rate was observed in patients treated approximately for 5–9 months than shorter duration [48] .

GLUCOCORTICOIDS

Glucocorticoids bind to the steroid receptor in the cytoplasm and translocate to nucleus where they bind to glucocorticoid response elements (GRE) on the DNA strand. Glucocorticoid receptors are also expressed in podocytes and translocate to the nucleus after steroid treatment. Thus glucocorticoids have a direct effect on podocytes in the treatment of nephrotic syndrome . Ransom et al. demonstrated that dexamethasone leads to increased expression of ciliary neurotrophic factor, heat shock protein 27 and αB-crystallin on podocytes.

CYCLOPHOSPHAMIDE

Cyclophosphamide is an alkylating agent that affects lymphocytes nonspecifically , hence more prone for infections.Twenty two percent of FSGS patients with steroid-resistance achieved remission due to cyclophosphamide in one study while others have shown a much lower effectiveness [49].

CYCLOSPORINE

Cyclosporine A (CSA) binds to cytosolic cyclophilin and inhibits protein phosphatase calcineurin .Thereby CSA blocks the signal transduction of factors like NFAT and NF-k B, essential for the induction of cytokines and activation of T-lymphocytes. CSA suppresses predominantly the cellular immunity and have minimal action on humoral pathway . Role of cyclosporine in FSGS is due to its direct effect on the filtration barrier by stabilising synaptopodin in the podocyte [50] .

In a randomized trial by National Institute of Health (NIH) ,12-month course of cyclosporine was compared with a combination of oral pulse dexamethasone and MMF in glucocorticoid- resistant children and adults up to 40 years of age [43] . Remission either complete or partial occurred in 46% of CSA group whereas only 33% achieved remission in the other group ,which was not statistically significant different .

TACROLIMUS

Tacrolimus is an immunosuppressive agent, that inhibits T cells activation[49] . It binds to a FKBP, a receptor in the cytoplasm of T cells and inhibit signal transduction.The effect of Tacrolimus in FSGS is probably by stabilising the slit diaphragm proteins.

MYCOPHENOLATE MOFETIL

Mycophenolate mofetil (MMF) is a prodrug and its active metabolite mycophenolic acid inhibits the inosine monophosphate dehydrogenase which is essential for purine synthesis . Role of MMF in steroid resistant cases of FSGS [51] are recently evaluated and found to be beneficial.

RITUXIMAB

Rituximab is a chimeric monoclonal antibody that targets CD20 on the surface of B cells and causes cell damage by complement dependent and

independent mechanisms. Case reports and small case series have shown benefit of rituximab in posttransplant recurrence of FSGS . Fresnedo et al [52] , showed a moderate response to rituximab in steroid resistant FSGS .

ORAL GALACTOSE

Savin *et al*. hypothesised that administration of large amounts of galactose to patients [36] with FSGS might cause formation of circulating complexes of free galactose and circulating factors that could be cleared by liver preventing these factors from interacting with the glycocalyx in GBM.

Apart from immunosuppression agents , supportive therapy like diuretics for edema, treatment of proteinuria with renin-angiotensin system blockade and control of blood pressure and hyperlipidemia should be given [53].

11.OUTCOME AND PROGNOSIS

In patients with primary glomerulonephritis, renal survival is clearly lower for FSGS than for IgA nephropathy and membranous nephropathy. Retrospective studies have suggested that complete remission may occur in up to 60% of patients after prolonged treatment with immunosuppressive drugs. Hence, a trial of steroid therapy is recommended in all patients with primary FSGS [54] .

Around 50% to 70% of FSGS patients may need regular dialysis or die due to uremia at 10 years after diagnosis. In one report , outcomes showed 30% of adult patients with idiopathic FSGS developing renal failure at 5 years . Massive proteinuria at the time of presentation or during the course carries a poor long-term prognosis. Age , raised serum creatinine at the time of diagnosis, hypertension, heavy smoking and advanced interstitial fibrosis are the factors that increase the risk for CKD [55] . The most powerful predictor of progression to CKD in FSGS is the treatment response . Male and African race confers 4-fold higher risk for ESRD progression . Wehrmann and colleagues [56] found an overall 10- year kidney survival of 67%.

Information about prognostic factors is useful to advise patients about the probable outcome of disease, selecting therapeutic options . Remission was associated with a 5-year renal survival of 94%, compared with 53% if remission was not achieved . The prognosis of untreated nephrotic patients is poor, with 50% developing end-stage renal failure within 8 years.

Prognosis is poor in patients not achieving remission, with 5 -year kidney survival of 65% (60–90%) and 10-year kidney survival of 30% (25–56%) [57] . Kidney survival rates were 90.4%, 69%, and 47% at 1, 5 and 10 years of follow-up in a cohort of children with FSGS [58] . Females have a better outcome than males in FSGS . Spontaneous remissions are very uncommon and

occur in less than 5% of patients [59] . Persistent nephrotic syndrome and renal insufficiency at presentation are independent risk factors for poor prognosis.

12.RENAL TRANSPLANTATION AND RECURRENCE:

Post-transplant FSGS recurrence is defined by histopathologic diagnosis ascertained before transplantation, profuse proteinuria appears early after transplantation ,and graft biopsy reveals the reappearance of FSGS weeks later. Recurrence occurs in 32% to 48% after transplantation .Thirty percent of patients with FSGS have recurrence of proteinuria after transplantation , and in 80% of those patients who have previous graft loss due to recurrent FSGS [60]. Recurrence of proteinuria may begin within 1 week after transplantation in around 70 % . Michelle A.Baum et al. showed six year survival after transplantation to be lower in FSGS with higher recurrence rate . Recurrence of FSGS often causes graft dysfunction (in 20 - 30% of patients) or graft loss (in 40 -50% of patients).

Age (younger) at onset of disease, non-black race, rapid progression to ESRD within three years , heavy proteinuria prior to transplantation, and previous allografts loss due to recurrence are risk factors for the recurence of disease [61] . Plasmapheresis or immunoadsorption have been shown to reduce proteinuria successfully and to interrupt the progression of renal insufficiency in recurrent disease in allograft.

METHODOLOGY

STUDY POPULATION

Adult patients (age group between 13-60) who were diagnosed to have biopsy proven FSGS and treated at Department of Nephrology at Rajiv Gandhi Government General hospital between 2006 January and December 2012 were included .

INCLUSION CRITERIA

All patients who have biopsy proven FSGS and treated with oral prednisolone for 24 weeks with atleast 6 months followup were included after getting written consent.

EXCLUSION CRITERIA

1. Patients with secondary causes of FSGS and those with family history FSGS and renal disease
2. Patients not willing for steroid therapy, poor compliance with drugs and followup with less than six months
3. Creatinine clearance less than 25ml/min/1.73$m^{2.}$

SUBJECTS AND METHOD

Demographics like age , gender, body mass index (BMI) , clinical symptoms and signs co-morbidities based on detailed history of the included patients were noted. Detailed clinical examination and blood pressure measurements were performed. Laboratory parameters included were 24-hr urine protein, urine examination findings , serum creatinine, blood urea, serum albumin and lipid profile at the onset of disease. Creatinine clearance (Crcl) was calculated with Cockraft Gault equation and expressed in ml/min/1.73 m^2.

RENAL BIOPSY

Renal biopsy was performed on all patients with adult onset nephrotic syndrome . The diagnosis of FSGS was made when at least one glomerulus show a typical sclerotic lesion in a segment in light microscopy. Renal biopsy tissue was processed for light microscopy and immunofluorescence. Subtyping of FSGS was performed in according to Columbia classification described by D'Agati. This include FSGS NOS, tip variant, perihilar variant, cellular and collapsing variant. Histologic features like global glomerulosclerosis, mesangial proliferation (>3 cells in a mesangial area, away from vascular pole) , intraglomerular foam cells and arteriolar changes (presence or abscence of arteriosclerosis) were studied . The interstitial fibrosis and tubular atrophy were graded as mild (<25%), moderate (26-50%) and severe (>50%) of cortical parenchymal involvement. Biopsies with significant staining for IgG and IgA

were excluded from the study. Clinicopathologic correlation were assessed based upon the renal biopsy findings after excluding secondary FSGS with extensive search for secondary causes.

TREATMENT AND FOLLOWUP

All patients are started on oral prednisolone 1 mg/kg/day after the infections were ruled out and continued for 6 months , tapered and stopped within one month. If the patients did not respond to steroids at 6 months, they were started on one of the following second-line drugs that include oral cyclophosphamide, cyclosporine, tacrolimus or MMF. All patients were received maximal tolerable dose of angiotensin-converting inhibitors (ACEI) or angiotensin II receptor blockers (ARB). HMG coenzyme A reductase inhibitor atovastatin 10-20 mg/day were also given. Supportive treatment like diuretics and antihypertensive drugs were also used whenever required.

All the subjects were monitored every two weeks for initial two months, monthly for next 4 months and quarter yearly thereafter. Patients were examined for the presence of edema, hypertension and infections at every visit. Any complications either due to disease process or treatment were noted. Urine routine, urine protein creatinine ratio and serum creatinine were monitored at each visit. Serum albumin, and fasting lipid profile were

monitored every 3 months. Total blood count was measured every two weeks if the patient was on cyclophosphamide or MMF therapy. Serum creatinine level were checked weekly in the 1st month, then fortnightly for six months and monthly thereafter for the patients receiving calcineurin inhibitors. When the patients relapse after complete or partial remission ,they were treated with steroids or second-line drugs.

DEFINITIONS USED

1. Hematuria – presence of > 2 RBCs in spun urine
2. Nephrotic proteinuria – urine protein > 3.5 gms/day
3. Hypertension – systolic blood pressure (BP) >140 mm Hg & diastolic BP > 90 mmHg
4. Anemia – blood hemoglobin < 11 gm/dl
5. Hypoalbuminemia – serum albumin < 3.5 gm/dl
6. Hypercholesterolemia – serum total cholesterol > 200 mg/dl
7. Renal failure – Crcl less than 60 ml/min/1.73 m^2
8. Complete remission (CR) - proteinuria <0.3 g/ day with a stable serum creatinine (<50% increase from baseline)

9. Partial remission (PR) - proteinuria between 0.3 g/day and 3.5 g/ day with at least 50% reduction in proteinuria from baseline and a stable serum creatinine

10. No remission (NR) – absence of complete or partial remission

11. Relapse - proteinuria >3.5 g/24 h after prior complete or partial remission

12. Chronic kidney disease – Crcl < 60 ml/min/1.73 m^2 after three months

13. ESRD - Crcl < 15 ml/min per 1.73m2 or the need for dialysis or renal transplantation.

TYPE OF STUDY

Simple retrospective and prospective study

STATISTICAL ANALYSIS

All the variables were expressed in mean ± SD or percentage. Univariate analysis was done by Fisher's exact and chi-square test for categorical variables and analysis of variance (ANOVA) was used for continuous variables. Statistical significant variables by univariate analysis were subjected to Linear regression analysis to assess multivariable association. Renal survival rate was determined by the Kaplan-Meier method . The log-rank test was used to evaluate the significance of the difference between survival mean in subgroups. In all analytic procedures, a p <0 .05 was considered significant .

ETHICAL CLEARANCE

Obtained from institute ethics committee

CONFLICT OF INTEREST

Nil

FINANCIAL SUPPORT

Nil

RESULTS

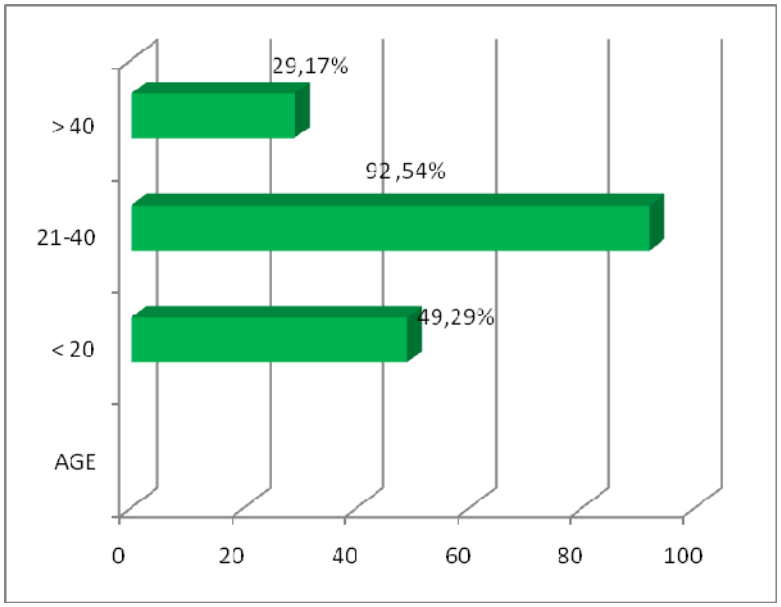
Among 195 adult patients (13-60 years) diagnosed to have biopsy proven FSGS between 2005-2012 , 170 were included in the study after applying exclusion criteria. In 25 excluded patients , five patients had stopped steroid therapy due to complications , four lost followup before six months and 16 patients had secondary causes of FSGS. Mean duration of follow up was 4.32 ± 1.2 years.About 65 % were males (Male:Female ratio - 111:59 ,1.9:1) . Baseline patient characteristics at the time of biopsy are shown in Table 1.

Table 1-BASELINE CHARACTERISTICS	**MEAN**	**S D**	**RANGE**
AGE (Years)	29.2	13.1	13-60
SYSTOLIC BLOOD PRESSURE(mm Hg)	132	45	90-220
DIASTOLIC BLOOD PRESSURE(mm Hg)	84	23	60-120
BODY MASS INDEX	24.7	13	20-29
PROTEINURIA(grams/day)	4.26	1.9	1.5-9
SERUM CREATININE(mg/dl)	1.24	0.56	0.6-5
CREATININE CLEARANCE(ml/min)	85.8	34	30-140
HEMOGLOBIN(gm/dl)	11.6	4.5	7-15
SERUM CHOLESTEROL(mg/dl)	215	111	118-540
SERUM ALBUMIN	3.4	0.7	2.5-4.2

AGE

The predominant age group in our study was between 21-40 years accounting for 54% of total patients . Figure 1 gives age distribution among study group.

Figure 1



CLINICAL PRESENTATION:

The most common symptom was edema (98%). Sub- nephrotic proteinuria (defined as urine protein < 3.5 gm/day) was seen in 35 patients (21 %). History of smoking was present in 27 patients (16%). Prevalence of anemia was 36%. Hypercholesterolemia and hypoalbuminemia were noted in 91

patients (54%) and 97 patients (57%) respectively.Type of clinical presentation are shown in below Table 2.

Table 2-PRESENTATION	NO OF PATIENTS (N-170)	PERCENTAGE
EDEMA	167	98
NEPHROTIC PROTEINURIA	135	79
SUB-NEPHROTIC PROTEINURIA	35	21
MACROHEMATURIA	2	1
MICRO-HEMATURIA	52	30
HYPERTENSION	70	41
RENAL INSUFFICIENCY	34	20

RENAL BIOPSY

All the patients underwent percutaneous renal biopsy . Mean number of glomeruli in the renal biopsy were 10 ± 2. Biopsy specimens with more than 10 glomeruli were considered adequate.Histological characteristics are given in Table 3.

Table 3-CHARACTERISTICS	**NO OF PATIENTS (%) N-170**
NO OF GLOMERULI >= 10	120(71)
GLOMERULAR SCLEROSIS ABSENT 0-25% 26-50% >50%	 106(62) 48(28) 13(8) 3(2)
MESANGIAL HYPERCELLULARITY	18(11)
PRESENCE OF FOAM CELLS	44(26)
INTERSTITIAL FIBROSIS &TUBULAR ATROPHY ABSENT <25% 26-50% >50%	 25(14) 97(57) 37(22) 11(7)
PRESENCE OF ARTERIOSCLEROSIS	94 (55)

In immunofluorescence, 90 patients (53 %) showed IgM positivity and 56 patients (33%) had C3 positivity usually 1 +.

TREATMENT

All the patients were started on antiproteinuric measures with angiotensin converting enzymes inhibitors (ACEI) or angiotensin receptor blockers (ARB) or both and escalated to a maximum tolerable dose ,out of which 14 patients (8%) were off drugs due to intolerance. Immunosuppression include oral prednisolone for all patients and second-line in steroid resistant patients whenever indicated and is given in figure 2.

Figure 2

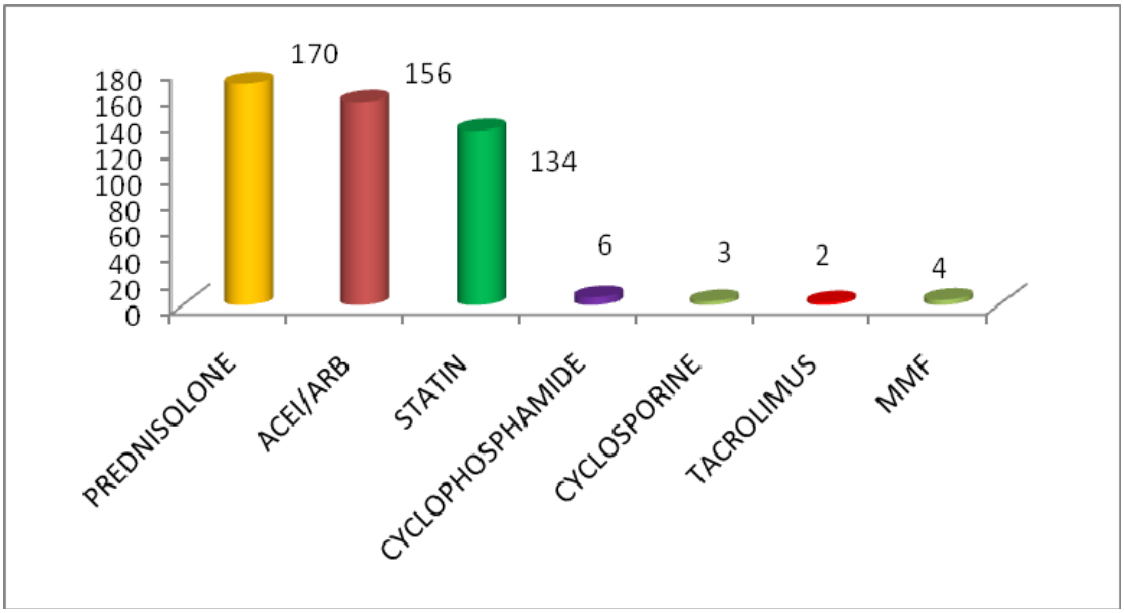
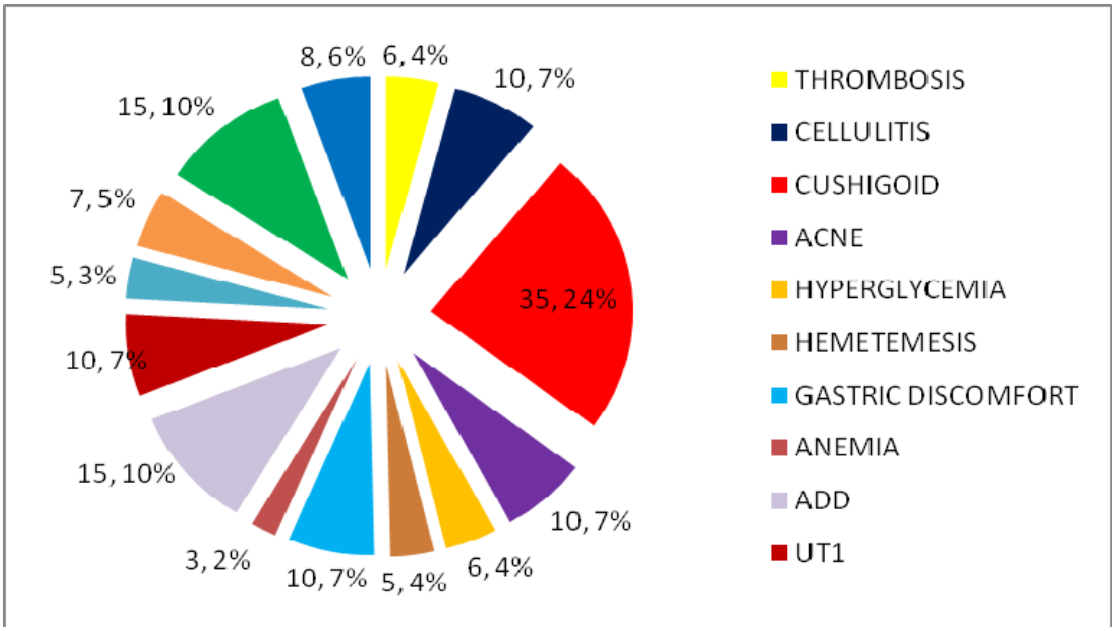


Figure 3



COMPLICATIONS

Venous thrombosis and cellulitis due to anasarca occurred as complications of disease process.Infection is the commonest complication followed by cushingoid features due to drugs. Two patient suffered from glaucoma and 8 from cataract due to steroid therapy. Complications during followup are summarised in figure 3.

FOLLOWUP AND OUTCOME

The mean followup duration was 4.32 years.Mean values of proteinuria , serum creatinine and creatinine clearance on followup are given in table 4.About 49 % of patient progressed to CKD at mean followup.

Table 4	**MEAN PROTEINURIA (gm/day)**	**MEAN CREATININE (mg/dl)**	**MEAN CRCL(ml/min/ 1.73 m2)**	**PATIENTS WITH CKD (%)**	**PATIENTS WITH ESRD cumalative %**
AT 3 MONTHS	2.18	1.13	87	21/170(12)	-
AT 6 MONTHS	1.67	1.43	83	22/170(13)	-
AT 12 MONTHS	1.5	1.28	78	31/165(19)	1(0.5)
AT 3 YEARS	-	1.7	64	47/111(42)	7(4)
AT 5 YEARS	-	2.1	55	46/76 (60)	25(15)
AT MEAN FOLLOWUP	-	2.35	58	84/170(49)	29(17)

Response to treatment as defined previously are expressed as CR , PR and NR and details of other immunosuppression therapy are described in Table 5. Incidence of ESRD is 29 (17%) at mean time of 4.32 years and two patients died due to uremia at mean time of 2.4 yrs.

Table 5	**NO OF PATIENTS(%)**	**MEAN DURATION(MONTHS)**
PREDNISOLONE		
PARTIAL REMISSION(PR)	OUT OF 170	
OVERALL	93(55)	4.5
PR ALONE	39(23)	5.7
PR FOLLOWED BY CR	54(32)	3.4
COMPLETE REMISSION	54(32)	6.4
NO REMISSION(NR)	77(45)	51
CYCLOPHOSPHAMIDE	OUT OF 6	
PR/CR	NIL	4
CYCLOSPORINE	OUT OF 3	
PR	2(66)	5.5
NR	1(34)	6
TACROLIMUS	OUT OF 2	
PR	2(100)	4.3
MMF	OUT OF 4	
PR	1(25)	8
NR	3(75)	12

RELAPSE

During followup, 13 patients out of 93 who achieved remission (CR or PR) had relapse at a mean duration of 2.8 years. Eighty percent of them had prior partial remission only .Table 6 gives details about relapse.

Table 6	NUMBER (%)
TOTAL NO OF PATIENTS	13(14%)
PATIENTS CHARACTERISTIC	
MALE	10(80)
ATTAINED CR	3(20)
ATTAINED PR	10(80)
ALONE ON STEROIDS	11(85)
ON CYCLOSPORINE	2(15)
TREATMENT	
2nd DOSE OF STEROID	5(38)
OUTCOME	
PARTIAL REMISSION	2(40)
NO REMISSION	3(60)

HISTOLOGICAL SUBTYPES OF FSGS

Among 170 FSGS patients, Not Otherwise Specified was the commonest , present in 96(56%) , followed by tip variant in 41(24%) , perihilar type in 16 (10%) and cellular 15(9%) . Only two (1%) patients had collapsing FSGS, reached ESRD in 2.2 years. Clinico-pathological details according to Columbia classification are noted in Table 7.

Table 7	NOS (96)	TIP (41)	CELLULAR (15)	PERIHILAR (16)
MEAN AGE	29	30	29	30
MALE /FEMALE	59/37(61/39)	29/12(70/30)	10/5(66/34)	11/5(69/31)
PROTEINURIA MEAN NEPHROTIC	 4.4 81(84)	 4.1 29(70)	 3.9 14(93)	 3.2 9(56)
HEMATURIA	29(30)	13(37)	6(40)	3(19)
MEAN SERUM CREATININE	1.16	1.32	1.17	1.6
RENAL FAILURE	16(16)	6(15)	4(26)	6(25)
HYPERTENSION	41(43)	14(34)	5(33)	9(56)
ANEMIA	36(38)	10(24)	9(60)	4(25)
HYPERCHOLESTEROLEMIA	52(54)	21(51)	9(60)	9(61)
HYPOALBUMINEMIA	52(54)	28(68)	99(60)	6(38)
IFTA	33(34)	14(34)	2(13)	5(31)
ARTERIOSCLEROSIS	51(53)	25(60)	9(60)	7(44)
REMISSION PR CR NR	 24(25) 23(24) 49(51)	 7(16) 22(54) 12(30)	 5(34) 4(26) 6(40)	 3(19) 5(31) 8(50)
AT FOLLOWUP CKD(<60ml/min) ESRD	 50(52) 17(17)	 13(32) 3(7)	 10(33) 1(6)	 7(44) 4(25)

Among subtypes , perihilar variant present with less microhematuria , nephrotic proteinuria compared to NOS($p<0.001$) and cellular variety($p<0.001$). Cellular variant present more with renal failure ($p<0.05$) at presentation Vs tip variant and more arterial hyalinosis in renal biopsy (p 0.03) compared to perihilar lesion. Hypoalbuminemia (p 0.001) was commonly seen in tip lesion and hypertension in perihilar variant (p 0.007) compared to other groups.

Interstitial fibrosis and tubular atrophy were seen more in NOS (p 0.007) Vs cellular variant. Complete remission was seen more in tip variant (p 0.001) when compared to others. Less remission and progression to CKD was increasingly noted in NOS type compared to tip lesion (p 0.003 & p 0.009 respectively).

PREDICTORS OF POOR RESPONSE TO TREATMENT

By univariate analysis of different variables , factors that predict poor renal response as denoted by nil remission are detailed in Table 8.

Table 8-FACTORS	p-VALUE
AGE < 20 YRS	0.9
MALE	0.8
NEPHROTIC PROTEINURIA AT ONSET	**0.01**
PERSISTENT NEPHROTIC AT 3 MONTHS	**<0.001**
PERSISTENT NEPHROTIC AT 6 MONTHS	**<0.001**
RENAL FAILURE AT ONSET	**0.03**
PERSISTENT RENAL FAILURE AT 3 MONTHS	**0.05**
PERSISTENT RENAL FAILURE AT 6 MONTHS	**0.01**
HYPERTENSION	0.5
RENAL BIOPSY	
GLOMERULOSCLEROSIS > 5 %	0.8
ARTERIOSCLEROSIS	0.12
INTERSTITIALFIBROSIS&TUBULAR ATROPHY(> 30%)	**0.007**
PRESENCE OF FOAM CELLS &MESANGIAL CELLULARITY	
IgM STAINING	0.5
	0.4
	0.3

Table 9-Independent variables	Coefficient	Std. Error	$r_{partial}$	t	P
(Constant)	-0.6428				
FIBROSIS	0.1700	0.06926	0.1888	2.455	**0.0152**
RENAL_FAILURE_AT_3M	0.1345	0.09958	0.1052	1.351	0.1786
RENAL_FAILURE_AT_6M	0.01073	0.007639	0.1093	1.404	0.1621
NEPHROTIC	0.08663	0.07975	0.08478	1.086	0.2789
NEPHROTIC_AT_3M	0.4151	0.07683	0.3898	5.404	**<0.0001**
NEPHROTIC_AT_6M	0.4263	0.1029	0.3087	4.143	**0.0001**

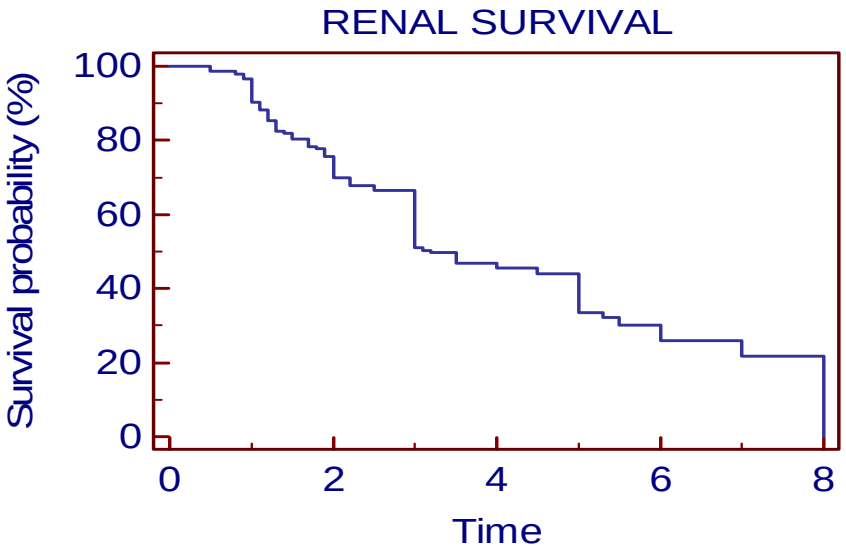
By multivariate analysis , persistent nephrotic proteinuria at 3rd and 6th month and presence of interstitial fibrosis and tubular atrophy > 30 % in renal biopsy are the independent predictors of poor renal response given in Table 9.

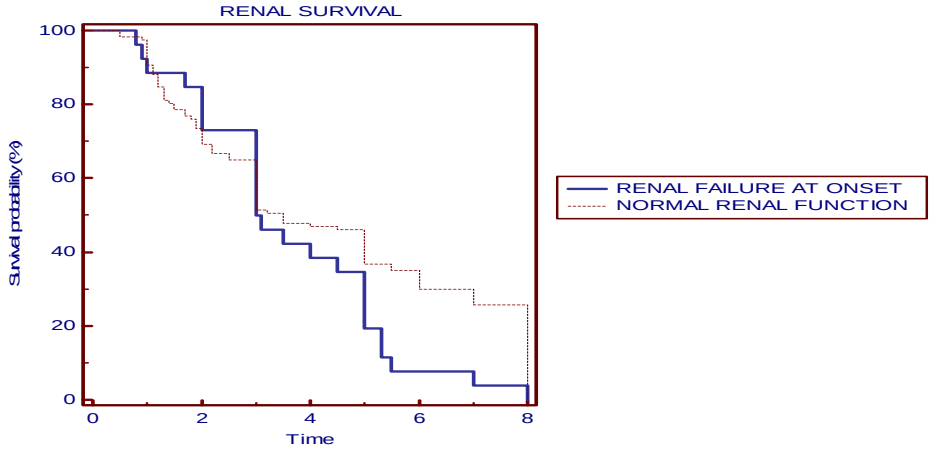
FACTORS PREDICTING CKD PROGRESSION AND POOR RENAL SURVIVAL

Analysis of factors like age < 20 years , male gender,nephrotic proteinuria at onset, persistent nephrotic proteinuria at 3 months and 6 months, renal failure onset,persistent renal failure at 3 months and 6 months,presence of anemia and hypertension , interstitial fibrosis and tubular atrophy > 30% and arteriosclerosis in renal biopsy and no remission after treatment were done using univariate to predict the progression to CKD and occurence of ESRD (poor renal survival). Subjecting the statistically significant variables to linear regression multivariate analysis,independent risk factors were derived. Details are given in table 10 with p values(<0.05 were considered significant).

Table 10-FACTORS	CHRONIC KIDNEY DISEASE		ENDSTAGE RENAL DISEASE	
	UNIVARIATE MULTIVARIATE (P VALUE)		UNIVARIATEMULTIVARIATE (P VALUE)	
AGE < 20 YRS	0.65	_	0.9	_
MALE	**0.05**	0.2	0.4	--
NEPHROTIC PROTEINURIA	**0.05**	0.9	0.6	--
PERSISTENT NEPHROTIC AT 3 MONTHS	**0.001**	0.4	0.2	--
PERSISTENT NEPHROTIC AT 6 MONTHS	**0.001**	0.2	**0.004**	**0.04**
RENAL FAILURE AT ONSET	**0.04**	0.6	0.2	--
PERSISTENT RENAL FAILURE AT 3 MONTHS	**0.0006**	0.1	**0.04**	0.4
PERSISTENT RENAL FAILURE AT 6 MONTHS	**0.0001**	0.6 0.5	**0.0001**	0.2 0.3
HYPERTENSION	**0.03**	**0.03**	0.3	0.1
ANEMIA	**0.006**	**0.0005**	**0.04**	**0.02**
NO REMISSION	**<0.0001**	**0.05**	**0.0001**	**0.0001**
INTERSTIAL FIBROSIS & TUBULAR ATOPHY	**0.0006**	--	**<0.0001**	---
ARTERIOSCLEROSIS	0.1		0.2	

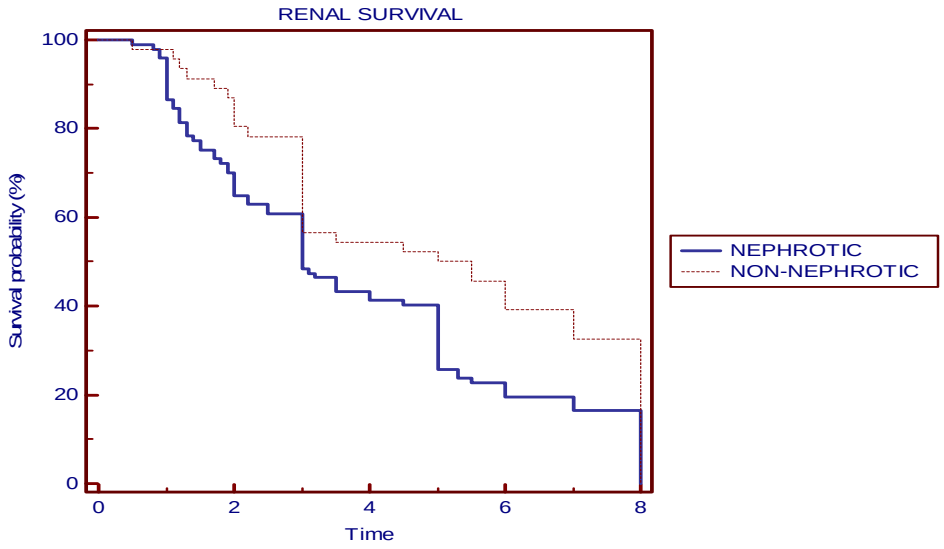
SURVIVAL ANALYSIS





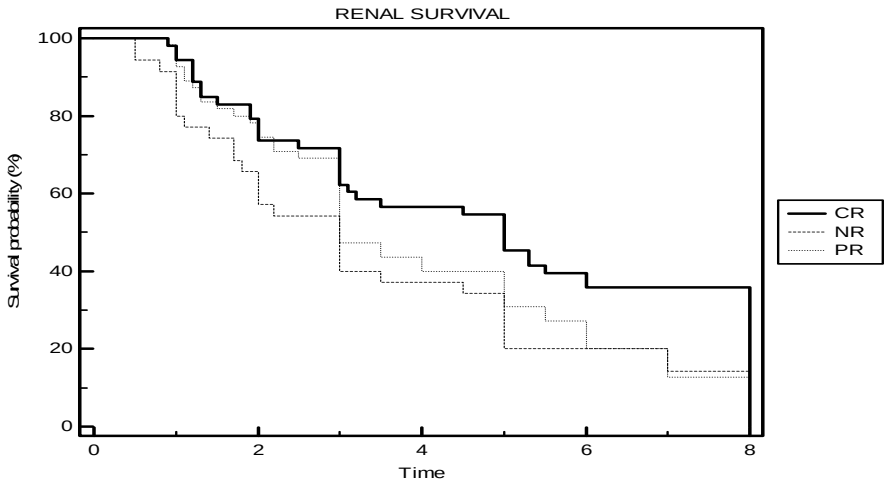
	Comparison of survival curves (Logrank test)	
Endpoint: Observed n	26.0	117.0
Expected n	19.3	123.7
Chi-square	3.3648	
DF	1	
Significance	P = 0.0536	

Survival analysis were done using Kaplan Meier method . Overall renal survival was 78 % at 3 years and 54 % at 5 years. Renal survival was significantly higher in patients presented with normal renal function compared with those with renal failure at presentation with 66 % Vs 42 % at 5 years .Renal survival difference with or without nephrotic proteinuria at onset was 39 % Vs 69 % at 5 years and is given below.



LOG RANK TEST-P (0.01)

In our study, renal survival at 5 years with complete remission was 69%, partial remission was 49% and no remission was 42%.There was no significant difference between those achieve partial remission and nil response.



LOG RANK TEST-P (<0.05)

DISCUSSION

Focal segmental glomerulosclerosis is a pathological process of various etiologies rather than a single disease entity, characterized by presence of segmental sclerotic lesions with focal involvement. The incidence of FSGS in adults is increasing recently [62] .One study showed FSGS as the cause of idiopathic FSGS in 15% of adult patients in 1970s, whereas in 35% of patients in 1990s and other studies showed prevalence of 30-35% in patients above 60 years [63] .

Among 170 patients, 111(65 %) were males ,similar proportion of males compared to other studies. Mean age in our study was 29.2 ± 13.1 years, predominantly in the age group of 20-40 and 17 % were above 40 years,while mean age in other studies was 35 to 45 years. Nephrotic proteinuria and microhematuria was present in 79 % and 30 % respectively. Approximately 75% of children and 60% of adult patients with FSGS present with nephrotic syndrome at as initial presentation [54].

Macro-hematuria was present in two patients. Hypertension was present in 41 % and renal insufficiency (Crcl < 60 ml/min/1.73m2) in 20 %. Around , 27 patients (16%) were smokers. Anemia was prevalent in 36%.

Hypercholesterolemia and hypoalbuminemia were seen in 91 patients (54%) and 97 patients (57%) respectively . Renal function at presentation depends on the severity of nephrotic syndrome and the duration of disease diagnosis and is seen in 20–25% [64] .

Singh et al [44] showed hypertension in 42.2% , gross hematuria in 36.4%, micro- hematuria in 63.6%, azotemia at the time of presentation in 37.5% . Mean proteinuria was 5.53 ± 2.89 gm / day while in our study it was 4.26 ± 1.9 gm /day . Taheri et al reported mean systolic BP of 121.19 mm Hg , dia-stolic BP of 77.52 mm Hg , serum creatinine of 1.18 mg/dL, plasma albumin of 3.29 g/dL, and GFR of 87.18 mL/min while in our study it was 132 mm Hg, 84 mmHg ,1.24 mg/dl , 3.4 mg/dl and 85.8 ml/min respectively.

Adequate renal biopsy specimen (> =10 glomeruli) was present in 71%. Global glomerulosclerosis was not seen in 38 % of patients. Mesangial hypercellularity and intraglomerular foam cells were present in 11% and 26 % respectively. Significant interstitial fibrosis and tubular atrophy was present (> 25% of cortical parenchyma) in 29 % of patients. Hyaline arteriosclerosis was seen in 94 patients (55%) . Total of 90 patients (53 %) showed IgM positivity and 56 patients (33%) had C3 positivity in immunofluorescence. Those patients with IgG and IgA positivity in renal biopsy were excluded from our study as other glomerular diseases like

membranous nephropathy ,IgA nephropathy ,diabetic nephropathy ,lupus nephritis and alport's syndrome also present as FSGS in renal biopsy. Schwartz et al [29] showed IgM positivity in 17 % and mesangial cellularity in 16 %. Global scars and synechiae to Bowman's capsule was shown to be prognostic factor in one study. Proteinuria induces integrin expression in the tubules and prognosis can be determined by integrin expression by immunochemical staining. Presence of mesangial hypercellularity and hyalinosis has been suggested as predictors for lower remission rate [66] .

All our patients received oral prednisoslone 1 mg per kg per day for atleast six months , tapered and stopped within one month . They were started on ACEI or ARB or both and escalated to a maximum tolerable dose , out of 170 patients , 14 (8%) were off these drugs due to intolerance. Benefit of ACEI and ARB may be due to inhibition of angiotensin II thereby inhibiting activation of TGF-b and matrix expansion.

Apart from steroids , six patients received oral cyclophosphamide, three received cyclosporine , two received tacrolimus and four received MMF for steroid resistance. Dose of cyclophosphamide is 2 mg/kg for 12 weeks and that of cyclosporine is 5 mg/kg daily for 12 months in addition to low dose steroids. During followup the incidence of renal failure (Crcl < 60 ml/min/1.73m2)s was

12% at 3 months,13 % at 6 months ,19 % at 12 months ,42 % at 3 years and 60 % at 5 years.Totally 49 % had renal failure at mean followup of 4.32 years. Incidence of ESRD is 29 (17%) at mean time of 4.32 years and two patients died due to uremia at mean time of 2.4 yrs.

On steroid therapy, out of 170 patients 54 patients (32%) had complete remission at mean time of 6.4 months, 39 (23%) had partial remission at mean time of 5.7 months and 77 (45%) had no remission. Partial remission occured earlier at mean time of 3.4 months (p 0.002) in those who achieved complete remission. Hence early partial response is the predictor of complete remission. Agarwal et al showed 58% remission (31% CR and 27% PR) to steroids in biopsy proven FSGS patients with nephrotic syndrome . Korbet et al reported a 50% response with oral prednisolone. Miyata et al 67 reviewed 32 FSGS patients with steroids alone . Forty-four per cent had CR, 12% had PR and 44% had nil response. In a study by Pei et al ,44 % had complete remission in median duration of 6 months with steroids in elderly patients (> 60 years of age) with FSGS. No relapses were noted and none had ESRD in the group who had remission .

None of the patients on cyclophosphamide therapy had remission either partial or complete.Two patients (66%) on cyclosporine and two patients (100%) on tacrolimus and one patient (25%) on MMF had partial remission

and none had complete remission. The prospective Regional Glomerulonephritis Registry Study [68] followed 95 adult and pediatric patients with FSGS, for a mean period of 61 months and showed a remission rate of 39 5 in adults prolonged therapy with steroids . Ponticelli et al reported an overall , 70% remission (complete or partial) and had stable renal function at 10 years with prolonged corticosteroids or immunosuppressive therapy.

A study cohort from the Toronto Glomerulonephritis Registry include 281 nephrotic FSGS patients .Out of them , 55 had CR, PR noted in 117, and 109 had no remission over a median follow-up of 65 months . One study described 52% of complete remission, 22% of partial remission and 26% of no response after 8 weeks of steroid therapy in primary FSGS patients with nephrotic proteinuria. Even partial remission was found to be an independent predictor of renal survival off dialysis.

Relapse occurred in 13 out of 93 patients (14%) who achieved remission (CR or PR) at a mean time of 2.8 years during followup compared in other studies where relapse rate was reported as high as 40%. Males (80%) had more relapse than females. Three patients (20%) and 10 patients (80%) respectively had complete and partial remission prior to the relapse. Two patients who achieved partial remission with cyclosporine had relapse during tapering of drug. Totally five patients who experienced relapse were treated with second

dose of steroids ,out of which two (40%) achieved partial remission at a mean time of 5.2 months and three didnot respond to treatment. A study showed relapse of 56 % after PR and associated with rapid decline in renal function compared with those who did not achieve PR[69] . Female sex and nadir of proteinuria during remission time were associated with a sustained remission.

Studies have suggested that cyclophosphamide and other cytotoxics may induce remission in additional 10% of patients who were steroid unresponsive [70-72]. Cyclosporine is the only agent tested for the benefits by randomized controlled trials in adults with FSGS [73] .The main drawback of CSA is that 40 to 75% experience a relapse within two months of stopping or tapering the drug. Patients on CNI therapy for at least one year before tapering experience sustained remission [74] . Cattran et al. [75] reported that 70% had remission by 26 weeks with 40% relapse at one year in patients who received CSA .

In a recent study of 25 patients with steroid-resistant FSGS, who were treated with tacrolimus (0.15 mg/kg/day) and full dose prednisone for atleast 8 weeks, CR was achieved in 40% and PR in 8% .Median time to remit was three months. Seventy six percent of patients relapsed after stopping tacrolimus[76] .

Briggs et al. reported a remission rate of 66% with MMF in steroid ressistant FSGS [77]. A study by Choi *et al*. noted the steroid sparing effect of MMF in these patients [78]. MMF is an alternative to CNIs in patients with progressive renal failure due to its negligible side effects on renal hemodynamics and metabolic profile.

Complications occur in FSGS as a part of disease or due to drugs. Corticosteroids may expose the patient to high risk of infections, hyperglycemia, cosmetic side effects, and hyperlipidemia . Osteoporosis is another potential adverse effect seen frequently and is severe in postmenopausal women .Venous thrombosis(4%) and cellulitis (7%) due to anasarca occurred as complications of disease process . Infection (48%) was the commonest complication followed by cushingoid features (24%) and hyperglycemia (4%) in our study.

Not Otherwise Specified is the commonest subtype of FSGS (according to working classification by D'Agati) and was present in 96 (56%) ,followed by tip variant in 41(24%), perihilar type in 16 (10%), cellular in 15(9%) and collapsing (1%). Thomas et al. showed a prevalence of cellular variant to be 3%. In one study, FSGS not otherwise specified was the most common subtype (44.6%), followed by perihilar FSGS (24.6%), collapsing (13.8%), tip (12.3%) and cellular FSGS (4.6%) [79]. The incidence in another series was tip lesion

(37%), NOS (32%) ,cellular variant (3%), perihilar variant (26%) , and collapsing variant(5%).

Among subtypes, perihilar variant present with less microhematuria (19%) , nephrotic proteinuria (56%) compared to NOS and cellular type. Cellular variant present more with renal failure at presentation (26%) Vs tip variant and more arterial hyalinosis (60%) in renal biopsy compared to perihilar lesion. Hypoalbuminemia was commonly seen in tip lesion (68%) and hypertension in perihilar variant (56%) compared to other groups. Interstitial fibrosis and tubular atrophy (34%) were seen more in NOS Vs other variant. Complete remission (54%) and better renal survival was seen more in tip variant when compared to NOS and perihilar variant similar to previous published studies . Less remission and progression to CKD was increasingly noted in NOS type (52%) compared to tip lesion.

The tip variant was associated with highest remission rate in our study of 70 % while other studies also showed higher remission rate of 57 – 60 %. Two patients with collapsing FSGS didnot respond to treatment, reached ESRD in 2.2 years. One study in 43 collapsing FSGS patients by Valeri and colleagues revealed nil response to oral prednisolone and rapid fall in kidney function.

There was no difference in mean age at presentation and gender ratio within the subtypes. Mean proteinuria in perihilar variant was 3.3 gm/day compared to other variant with mean of 4.2 gm/day.Mean serum creatinine was also higher in perihilar variant compared to others (1.5 mg/dl Vs 1.22 mg/dl).

By multivariate analysis , persistent nephrotic proteinuria at 3rd and 6th month and presence of interstitial fibrosis and tubular atrophy > 30 % in renal biopsy are the independent predictors of no remission after treatment. Presence of nephrotic proteinuria at onset, renal failure at onset, persistent renal failure at 3 months and 6 months were significant risk factors for poor treatment response predicted by univariate model but not by linear regression analysis. Most studies demonstrated that presence of significant interstitial fibrosis was the only independent predictive factor for response to treatment.

One study from Europe showed a spontaneous remission rate of 23% in patients with FSGS not treated with immunosuppression [80] .This may be due to various aetiology of FSGS , better BP control and liberal use of antiproteinuric measures. Achievement of sustained CR or atleast PR ,retard progression rate and improving renal survival are important goals in management of FSGS.

Risk factors like male gender, nephrotic proteinuria at onset, persistent nephrotic proteinuria at 3 months and 6 months, renal failure onset, persistent renal failure at 3 months and 6 months, presence of hypertension , anemia , interstitial fibrosis and tubular atrophy of > 30% in renal biopsy and no remission after treatment predict the progression to CKD at mean followup.Of this last three factors were the independent predictors. Absence of remission was the single most strong predictor for the progression to chronic kidney disease.

Predictors for the occurrence of ESRD at mean followup time were persistent nephrotic proteinuria at 6 months, persistent renal failure at 3 months and 6 months, presence of anemia , interstitial fibrosis and tubular atrophy of > 30% in renal biopsy and no remission after treatment . Persistent nephrotic proteinuria at 6 months, interstitial fibrosis and tubular atrophy > 30% and no remission after treatment were found to be independent risk factors. Strong predictor for progression to ESRD in our study was the presence of interstitial fibrosis and tubular atrophy > 30% in renal biopsy. Rydel et al found that the extent of interstitial fibrosis predicted the development of ESRD [81] . Wehrman et al found that interstitial fibrosis, not serum creatinine, had independent predictive value for progression to ESRD [56] . Korbet et al showed that serum creatinine > 1.3 mg/dl, range of proteinuria and interstitial fibrosis > 20 % were positive predictors of occurrence of ESRD.

Overall renal survival by Kaplan Meier survival analysis was 78 % at 3 years and 54 % at 5 years. Renal survival was significantly higher in patients presented with normal renal function compared with those with renal failure at presentation with 66 % Vs 42 % at 5 years. Renal survival difference with or without nephrotic proteinuria at onset was 39 % Vs 69 % at 5 years . Renal survival differ from those who respond to treament than those who didnot achieve remission (either complete or partial). But in our study, renal survival at 5 years for complete remission was 69%,for partial remission 49% and for no remission 42 %.There is no significant difference between those achieve partial remission and nil response.Therefore, attaining complete remission significantly improves renal survival. Renal survival rates were 68.6% and 27.3% at five and 10 years respectively in a study by Singh and colleagues [42] . Cameron et al [82] reported five and 10 year survival rates as 70% and 40% respectively.

CONCLUSION

1. Males were more commonly affected with FSGS and mean age at presentation in our study was 29.2 ± 13.1 years.

2. The incidence of nephrotic proteinuria was 79% and microhematuria was 30 % .Hypertension was present in 41 % and renal insufficiency in 20 %.

3. Complete remission was seen in 32% at a mean time of 6.4 months, partial remission in 23 % at a mean time of 5.7 months and 45% had no remission.

4. Partial remission occurred earlier at a mean time of 3.4 months in those who achieved complete remission.

5. Relapse rate was 14% at a mean time of 2.8 years during followup .

6. FSGS- NOS was the commonest subtype of FSGS (present in 56%) ,followed by tip variant in 24% , perihilar type in 10%, cellular in 9% and collapsing in 1%.

7. Cellular variant present more with renal failure and more arterial hyalinosis in renal biopsy.

8. Perihilar variant present with less microhematuria ,nephrotic proteinuria and more with hypertension compared to other variants.

9. Tip lesion present with more hypoalbuminemia and complete remission (54%) and renal survival was seen more in this variant.

10. NOS was characterised by more interstitial fibrosis and tubular atrophy ,less remission and more progression to CKD compared to tip variant.

11. Persistent nephrotic proteinuria at 3^{rd} and 6^{th} month and presence of interstitial fibrosis and tubular atrophy > 30 % in renal biopsy are the independent predictors of poor response to treatment.

12. Male gender, nephrotic proteinuria at onset, persistent nephrotic proteinuria at 3 and 6 months, renal failure at onset, persistent renal failure at 3 and 6 months, presence of hypertension , anemia , interstitial fibrosis and tubular atrophy of > 30% in renal biopsy and no remission after treatment predict the progression to CKD.

13. Absence of remission was the single most strong predictor for the progression to chronic kidney disease.

14. Persistent nephrotic proteinuria at 6 months, interstitial fibrosis and tubular atrophy > 30% and no remission after treatment were found to be independent risk factors and presence of interstitial fibrosis and tubular atrophy > 30% in renal biopsy was the strong predictor for development of ESRD in our study.

15. Overall renal survival was 78 % at 3 years and 54 % at 5 years. Renal survival difference with or without nephrotic proteinuria at onset was 39 % Vs 69 % at 5 years.

16. Renal survival was significantly higher in patients presented with normal renal function compared with those with renal failure at presentation with 66 % Vs 42 % at 5 years.

17. Renal survival at 5 years for complete remission was 69%,partial remission was 49% and no remission was 42 % .

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S.NO	NAME	AGE	SEX	PROTE	SR.CR	SBP	DBP	HB	T.C	SR.AL	NO. O	GLO	TYPE	FIBRO	ART H	IGM	C3	COMPL	PCR 3N	CR3M	PCR.6	CR.6M	PCR 1	CR.12	TIME -	TIME -(	RELAPSE	TIME	CR.3Y	CR.5Y	FOLLO	ESRD
1	NAVANEETHAM	56	F	4	1.1	156	80	7.6	190	4	24	3	NOS	50	Y	N	N		2	1.2	0.5	1.1	0.3	1	12	16					1.3	
2	RAJESH	15	M	4.5	0.9	130	80	7.7	160	3.2	9		TIP	20	N					1									1.1	1.3	12	
3	PARASURAMAN	45	M	1.8	1.2	110	70	14.5	200	3.1	9	2	NOS	10	N	1+	N		1.1	0.8	0.08	0.9	0.1	0.9	2	4			1	1.2	12	
4	DURAIRAJ	29	M	2.8	1.1	140	80	12.6	206	3.8	2		NOS	10	Y	2+	N		0.9	0.8	0.12	0.8	0.11	1					1.2	1.3	13	
5	HAJIRA	22	F	2.8	0.9	140	100	9.9	210	3.5	2		CELLULAR	20	N	2+	N		2	0.9	1	1	0.8	1	24				1.2	1.2	13	
6	ANTONY	37	M	3.4	0.7	136	98	12	245	3.3	3		TIP	0	N	N	N	CUSHING	0.8	0.7	0.1	0.9	0.08	1	4	8			1	1	15	
7	GOPIKRISHNAN	36	M	4.3	1.7	190	90	11	300	3.4	11	3	NOS	50	Y	2+	N	CUSHING	2.4	2.3	1.1	2.5	1	2.8	24				3.4	4.5	7	6
8	KAMALA	28	F	7.7	0.8	128	80	9.8	258	3.3	9		NOS	50	Y	1+	N		2.3	0.9	1.2	1	0.8	1.2	12	28			1.2	1.5	14	
9	NARAYANAN	40	M	3.9	0.9	130	90	11	196	4	5	1	CELLULAR	20	N	1+	N		1.9	0.8	1.1	1.2	0.1	0.8	24	34			1	1.2	13	
10	FARID AHAMED	18	M	5.8	0.8	90	70	12.8	230	3.2	10	2	TIP	20	N	N	N	CUSHING	0.3	0.8	0.08	1	0.1	1	2	5	2	2,4	1.2	1.3	14	
11	SARAVANAN	47	M	3.1	0.9	100	70	13.9	245	3.3	4		NOS	0	N	2+	2+		2	0.9	1	1	1	1	12	20					2	
12	SANKAR	37	M	2.6	0.7	110	70	13.2	300	4	1		NOS	30	N	1+	N		3	1	3.2	1.2	2.1	1.9					1.9	3	14	14
13	VELAYUTHAM	14	M	4.5	0.8	110	70	12.8	245	2.9	20		CELLULAR	20	N	1=	2+		2	0.8	0.8	1	0.12	1	14	24			1.1	1.4	16	
14	MOHANDOSS	18	M	3.8	0.9	110	70	11.5	279	4	15		TIP	20	Y	1+	4+	CUSHING	0.8	1	0.18	1	0.1	1.1	12	20	1	6	1	1	8.5	
15	RAJASEKAR	13	M	3.2	0.9	110	70	13.8	180	3.7	6		NOS	0	N	N	N		1.2	1	0.3	1	1	1	10	22			1		3	
16	POONGULALI	30	F	2.6	2.2	180	90	12	180	3	2		TIP	50	N	2+	N	CUSHING	1	2.1	0.5	2.4	1	3.4	10				4.5	5	6	5.5
17	JAMUNA	40	F	4.1	0.7	150	90	10.8	345	3.4	4		NOS	20	Y	N	N	ACNE	2.3	0.8	1.2	1	1	1	3						1	
18	MUTHU	35	M	5.6	1.1	140	100	11	133	3	20		NOS	0	N	N	N		0.8	0.8	0.15	0.8	0.12	1	2	3					1	
19	MANJULA	37	F	5.46	0.8	150	90	12	217	4	10	1	PERIHILAR	20	N	1+	N	CUSHING	1.2	0.8	0.3	1	0.2	1	3	5					1.2	
20	GOVINDHAN	19	M	3.7	0.7	110	70	14	245	4.2	4	1	NOS	0	N	N	N		0.3	0.8	0.3	0.8	0.2	0.8	1	3						
21	SAMRUTH BEGAM	42	F	3.4	1	140	90	11	234	3.3	16	6	NOS	20	N	1+	1+			0.8												
22	NAGAN	18	M	6	1.5	160	100	13.2	209	3.7	20		PERIHILAR	10	N	N	N			0.8												
23	BALAMANI	29	F	4.22	1	120	90	9.8	197	4	9	1	CELLULAR	20	Y	1+	1+		0.3	1	0.12	1	0.1	1.1	1	2			1.1	1.4	10	
24	RAJENDRAN	40	M	4.3	0.8	130	90	11	245	3.4	8	1	NOS	0	N	N	N		0.2	0.8	0.12	0.8	0.12	1	2	2.5					1.2	
25	MOHANA	25	F	2.7	0.9	110	70	10.2	250	3.4	6		NOS	40	Y	1+	1+		0.5	1	0.3	1	0.2	1	4	6	2	2,4	1	1.1	6	
26	SASIKALA	26	F	3.76	0.9	140	100	8.8	260	3.4	7		CELLULAR	10	Y	N	N		3	1	3.2	1	2.9	1	NO				1.3	1.5	5	
27	KOWSALYA	49	F	2.6	1	150	90	13.2	270	4	7	4	PERIHILAR	30	Y	N	1+		2.5	1.1	2.5	1.2	2	1.5	NO				2.2	6	6	5
28	KRISHNAMOORTH	23	M	2.34	1	120	90	9.8	195	3.3	7		NOS	0	N	N	N		2.3	1	2.2	1.2	2	1.2	NO				1.3	1.7	12	9
29	BHARATHY	40	F	3.3	0.9	120	80	10	255	4	7		TIP	20	N	1+	1+		3	1	2.9	1	3	1.2	NO				2.1	3.1		
30	VIJAYALAKSHMI	33	F	1.6	2.1	150	90	8.8	216	3.5	4		PERIHILAR	30	Y	N	N		2	2	1.2	2	1.1	2	6				2.9	3	12	9
31	AYYANAR	21	M	5.3	1.1	110	80	11.4	189	3.5	16	1	CELLULAR	10	Y	N	N		0.8	1	0.2	1	0.12	1	2	4			1.1	1.1	16	
32	SARASWATHY	27	F	2.9	1.2	160	100	9.2	234	3.7	12	4	NOS	20	Y	N	1+		1.2	2	1.1	1.9	1	2	6						1.1	
33	RAMAN	33	M	3.4	1	140	90	10	234	3.1	20	2	CELLULAR	20	Y	N	1+		2.3	1	1.5	1	1	1.1	6							
34	BABU	43	M	4	1	140	90	11	212	3.5	12	2	NOS	10	Y	N	N		2	1	2	1.1	1.9	1	NO				1.4	1.5	13	
35	EDISON	28	M	3.7	1	120	80	11.2	200	3.3	9		NOS	20	Y	N	N		3.3	1	3.4	1	2.8	1.1	NO				1.4	3	5	5
36	SAROJINI	30	F	3.4	1	150	90	11	190	3.6	14		CELLULAR	20	Y	2+	3+	CUSHING	3	1	2.9	1	2.9	1.2	NO				1.3	2.2	9	
37	REENA	30	F	3.1	1	150	90	11	234	3.3	6	1	NOS	30	Y	1+	2+	CUSHING,	2.9	1	2.9	1.1	2.6	1.1	NO				1.6	1.9	9	
38	PONRAJ	16	M	2.7	0.7	130	90	13	190	3.7	8	1	NOS	20	Y	1+	2+		3	1	1	1	0.8	1.1	6				1.2	1.6	9	
39	BHASKAR	31	M	3	1.2	140	96	9.2	180	3.5	15	2	NOS	10	Y	N	N		0.6	0.8	0.12	1	0.1	1	2	4			1	1.2	8	
40	ANNADURAI	35	M	3.3	0.9	110	70	13.9	188	4	6		NOS	10	Y	2+	3+		1.8	1	0.9	1	1	1	6		2	4,6	1	1.5	8	
41	VEDIAPPAN	20	M	2.7	1.2	110	80	12.6	260	3	8		TIP	0	Y	N	N		2.5	1	2	1	2.2	1	NO				1.2	1.5	8	
42	KRISHNAN	40	M	4	1	110	70	12.8	290	2.8	7		TIP	50	Y	1+	3+		0.5	0.89	0.13	0.9	0.1	1	2	4			1	1.1	8	
43	VISWANATHAN	15	M	4	1	110	70	9.2	188	4	7	2	NOS	20	Y	1+	2+		2.5	1	2	1	2	1	NO				1.5	1.9	8	
44	SRINIVASAN	37	M	3.5	1	110	70	13	220	3	12		NOS	0	Y	1+	N		0.2	1	0.12	0.9	0.12	1	1	1.5			1	1.2	8	
45	SUDAMANI	47	M	3.75	1	160	100	11	280	3.2	9	1	NOS	50	N	1+	2+		2.2	1	2.3	1	2	1.2	NO				1.9	3	8	6
46	SHANMUGAM	26	M	3.7	1	110	80	11.4	188	3.6	8		NOS	0	N	1+	N		0.9	1	0.12	1	15	1.1	2	6			1.2	1.2	8	

47	SIVASAKTHI	13	F	4	1	110	70	11	190	3.3	8		NOS	10	N	N	N		2.2	1	1.4	1	1	1	6		1	3	1.6	3	6	
48	PALANI	26	M	3.4	1	120	80	13.8	170	4	4		NOS	10	Y	1+	1+		3	1	3.1	1	2.7	1	NO				1.5	1.9	6	
49	BENAZIR PARVEEN	15	F	6.32	1	120	80	10.3	190	3.4	7		NOS	50	Y	1+	1+		3	1	3.4	1.3	3	1.7	NO				1.9	2	6	6
50	SRINIVASAN	27	M	5.4	1.1	120	80	12.8	150	4	13	1	NOS	0	N	1+	N		3.8	1	3.5	1.1	3	1.2	NO				1.7	2	6	
51	SHAMSUNDAR	13	M	2.4	1	120	80	11	190	3.6	5		NOS	0	N	N	N		1.2	1	0.2	1	0.12	1.1	2	4			1.2	1.1	6	
52	RAJASEKAR	32	M	5.7	1	150	90	11.4	154	3.4	17	1	TIP	30	Y	1+	2+	SEPSIS	5.5	1	5	1.1	4.5	1.2	NO				1.5	1.7	6	
53	LALITHA	27	F	4	1	160	90	14	202	3.3	5		NOS	0	N	N	N		3	1	3	1	3	1.1	NO				1.7	5	6	5
54	PARASURAMAN	27	M	3.29	1.1	160	90	14.2	176	3.4	12		NOS	30	Y	2+	2+	CUSHING	3	1	2.9	1	2.3	1.2	NO				1.2	1.7	6	
55	THARANI	16	F	4.5	1.2	160	100	11	190	3	7	1	NOS	30	Y	2+	3+	ACNE	3.3	1	2.9	1.1	2.2	1.1	NO				1.9	2.2	6	
56	LIVIYA	17	F	3.7	1.1	90	60	12.8	130	3.9	11		PERIHILAR	0	N	2+	4+	ACNE	2.1	1	1.1	1	0.8	1.1	6				1.2		4	
57	GUNASUNDARI	16	F	5.4	0.9	130	90	11	240	4	3		NOS	20	Y	2+	N		1.1	1	0.12	1	0.2	1	2	4			1.3		4.5	
58	KALAIARASI	23	F	7	0.9	140	90	12	267	3.5	10		NOS	20	Y	1+	N	TB ADENI	4.5	1	4	1	3.7	1.2	NO				1.6		4.5	
59	NEELAMEGAM	58	M	3.46	1.8	180	100	11	230	3	10	3	PERIHILAR	40	Y	1+	N		3.5	1.9	3.2	2	3	2.3	NO				5.7		4.5	3.5
60	SUDHANDHIRAJ	42	M	4	1.5	150	100	10	345	3.1	12	2	NOS	30	Y	1+	N			0.8												
61	KRISHNAMOORTH	20	M	4.5	1.2	140	90	12	220	3.3	3		TIP	20	Y	1+	1+		2.5	1	1.7	1.1	1.2	1.1	6						1.7	
62	THANGABATHRAK	28	F	5	0.8	120	80	14	230	3.4	10		NOS	10	Y	N	N		2.6	1	1.8	1.1	1.7	1.2	5						1.7	
63	VASANTHI	41	F	3.7	1	120	80	11	220	3.5	11		NOS	10	Y	1+	N		2.8	1.1	2.5	1.2	2.2	1.2	NO						1.9	
64	PRAVEENKUMAR	14	M	6	1	120	70	12	240	2.8	13		NOS	10	Y	1+	N		3.8	0.9	3.4	1	3	1.2	NO						2	
65	NATARAJAN	70	M	5	1.4	160	80	11	230	3.4	4		CELLULAR	40	Y	N	N	CUSHING	3.4	1.4	3	1.3	2.9	1.4	NO						2	
66	KANAGARAJ	18	M	2.7	0.8	130	90	14	195	3.5	18		TIP	30	Y	N	N	CUSHING	2	1.1	2	1	0.12	1.1	3	4	1	1.5			2	
67	KUMARESAN	17	M	5.73	1.5	120	90	14	140	3.2	20		TIP	10	N	1+	1+	CUSHING	2.5	1	1.7	1.1	1.6	1	4						1.4	
68	BALU	16	M	4.1	1.2	140	90	13	200	3	9		PERIHILAR	10	N	N	N	DISCON	3	1.1	3.1	1.1	3	1	NO						1.3	
69	RAMAN	33	M	3.5	2.7	130	90	11	210	3.1	20		CELLULAR	10	N	N	1+		3.1	2	3.2	1.4	2.7	2	NO						1.7	
70	MANIVANNAN	35	M	5.8	2.3	140	90	13.8	220	3.4	11		TIP	15	N	N	N		1.2	1	0.2	0.9	0.12	1	2	3.5					1.3	
71	PASUPATHY	15	M	1.2	0.8	120	80	12.8	170	3.8	21		NOS	10	N	N	N		1.3	1	1	1	1.1	1	NO						1.3	
72	SARASWATHY	26	F	6.1	1.3	120	80	11.2	240	3.4	12	4	NOS	30	N	N	N		3	1.2	3	1.2	2.9	1.3	NO				2		4.8	
73	YAMUNA	13	F	5.3	0.7	130	80	11	190	3.7	4		NOS	20	N	1+	1+			0.8											LOST	
74	VALARMATHY	35	F	6.5	1.8	170	100	11	230	3.6	16	1	NOS	20	Y	N	N		2.7	1.7	3	2.2	2.3	3	NO				3.4		4.8	4.5
75	GOPI	25	M	4.5	1.4	130	90	12	210	3.9	4		TIP	40	Y	2+	1+		1.2	1	0.2	1	0.2	1	2	3.5					4.8	
76	SANGEETHA	13	F	5	1.1	110	70	13	200	3.6	26	1	NOS	10	N	N	N		3	1.1	2.9	1.1			NO							
77	VASANTHA	28	F	4	1	140	80	12	196	4	20	1	TIP	20	N	1+	2+		2	1	0.2	1	0.12	1	2	4			1.4	2.4	8	
78	SUNDARI	30	F	3.7	1.4	140	80	9.8	180	3	6		TIP	20	N	1+	1+		3	1.1	2.8	1	2.6	1.1	NO				1.1	1.2	8	
79	DILLIGANESH	14	M	3	0.9	120	80	12	180	3.6	4		NOS	20	N	N	N		3	1.2	2.9	1.1	2.5	1.3	NO				1.7	2.2	8	6
80	GOPI	17	M	2.6	0.9	120	80	12.6	220	4	5		PERIHILAR	20	N	1+	1+	CUSHING,	3	1.2	2.3	1.3	2.5	1.9	NO				5		5	5
81	MANI	45	M	3.2	1.3	150	80	8.2	188	3.6	9	1	PERIHILAR	10	N	N	N		1	1	0.2	1	0.2	1	2	4			1.2	1.5	8	
82	SRINIVASAN	34	M	2.9	1	140	90	12	196	3.6	7	1	PERIHILAR	10	N	1+	N		0.9	1	0.12	1	0.2	1	1	3.5			1.3	1.8	8	
83	MANIKANDAN	16	M	4.5	0.8	110	70	12	290	3	8		NOS	10	N	1+	N		0.8	1	0.12	1	0.2	1	2	5			1.4	1.9	8	
84	SUSEELA	40	M	3	1.2	110	70	11.5	180	3.2	24	2	NOS	10	N	1+	N		1	0.9	0.15	1	0.12	0.9	2	5			1	1.1	8	
85	SAIRAM	13	M	5.9	0.7	120	70	12.1	247	3	6		NOS	10	N	2+	N	CUSHING,	3.5	0.8	2.9	0.8	3	1	NO						2.2	
86	KANNAN	30	M	2.6	2	130	80	13.8	120	3.4	10	1	TIP	20	Y	N	N		2.8	1.4	1.9	1.4	1.5	1.3	6						2.2	
87	KATHIRAVAN	20	M	4.7	1.3	130	100	14.9	310	3	6		TIP	20	Y	N	2+	CUSHING,	3	1.2	2.9	1.1	2.5	1.3	NO						2.6	
88	PAPPAYEE	55	F	2.6	1.4	160	90	9	270	3.8	3	1	NOS	20	N	N	N			0.8												
89	RAGHUPATHY	47	M	3.7	1.1	110	80	8.8	240	3.1	4	1	TIP	40	N	1+	N		1.2	0.9	0.12	1	0.12	1	2	3.5					2.6	
90	MARIASELVAM	30	F	4.3	0.7	110	70	12.5	249	3.7	15	1	NOS	40	Y	3+	2+	CUSHING	2.5	1	2.2	1	2	1	NO						2.6	
91	VARADHAN	64	M	1.6	2	120	80	15.8	270	3.4	9	1	TIP	30	Y	2+	N	CUSHING	1.2	1	1	1	1.2	1	3						2.6	
92	SHANATHI	35	F	4.3	3.5	160	100	10	118	3.7	3	1	NOS	60	Y	4+	4+		3	3	2.6	3.8	2	4	2	4.5						
93	MADHAN	19	M	4.4	1.4	170	100	6	130	4	14	2	NOS	40	Y	N	N		3	1.3	2.8	2	3	2.1	NO						2.9	2.4

94	SYED	23	M	3.2	0.9	170	120	11	220	3.5	16	1	NOS	20	N	2+	N			0.8											
95	GOMATHY	33	F	3	0.8	140	90	11.8	130	4	9	1	NOS	30	N	N	N		0.2	0.8	0.12	0.9	0.1	0.9	1	3					1.9	
96	IMRANKHAN	17	M	4	0.8	120	80	11	230	3.5	8		TIP	20	N	N	N		1.9	0.8	0.2	0.9	0.2	0.9	2	6			1		5	
97	VIRUTHAMBAL	42	F	4.6	1.9	150	90	10	230	3.3	10	2	NOS	30	N	N	N		3	1.9	2.9	2	2.5	2.1	NO				2.9		3	
98	PRASANNA	16	F	4	1.6	150	90	10	140	3.3	17	1	NOS	30	N	2+	N		2.9	2	2.8	2.1	2.5	2.2	N0				3		5	
99	SALEEM	19	M	2.7	0.7	130	80	12.5	220	4	18	1	TIP	20	N	2+	N		1.2	0.7	0.2	1	0.2	1	1	4			1		3	
100	JEYANTHI	40	F	6.1	2	150	90	12	210	3.5	9	2	TIP	20	Y	N	N		1	1.5	0.2	1	0.2	1	2.3	4.5					2	
101	MURALI	14	M	4.3	1	130	80	11	220	3.4	10	2	NOS	30	Y	N	N		3	1	2.9	1.1	2.5	1.1	NO				1.2		5	
102	SALEEM	13	M	4.1	0.7	120	80	11.8	470	3.1	9	2	PERIHILAR	30	Y	N	N		1	0.8	0.23	1	0.2	1.1	2	4					1.9	
103	SANGEETHA	13	F	5	1.3	110	70	13	220	3.6	26	2	NOS	10	N	1+	N		1	1	0.2	1.1	0.2	1	3	5					0.9	
104	VATCHALA	45	M	3.1	0.7	110	70	12	260	3	10	2	CELLULAR	20	N	2+	2+		2	1	0.9	1	0.8	1.1	6				1.6		6.9	
105	VINOTH	23	M	3.7	1.8	150	90	10	240	3.4	10	1	NOS	20	N	1+	N		2	1.6	1.7	1.5	1	2	5				6		3	3
106	GOTHANDARAMAN	38	M	5.3	2.1	150	100	12.8	120	3.4	6	3	NOS	50	N	N	N		2	1.8	1.8	2	1	2.1	NO						1	
107	ARUNKUMAR	37	M	8	1.2	140	90	12	220	3.2	10		TIP	0	N	N	N		0.12	0.8	0.2	0.8	0.2	0.8	1	2					1	
108	GAJENDRAN	52	M	9	3.4	160	100	9.8	120	3	5	2	NOS	20	Y	N	N		2	2	1.8	2			5						0.8	
109	ILAYADASAN	18	M	5.5	1.1	150	90	9	220	3.4	9	1	NOS	20	Y	1+	N		2.3	1.2	2.2	1.2	2.2	1.4	NO				1.7		6.4	
110	MARIA LOUIS	30	M	2.6	1.2	110	70	14	294	3.5	9	2	TIP	10	Y	1+	N		2.2	1	2.2	1	2	1.1	NO				1.5		3	
111	KUMARAVALLI	46	F	4.8	1.8	140	90	10	130	3.8	15	6	NOS	40	Y	1+	N			0.8											
112	SHANMUGAM	50	M	6.5	1.8	140	90	14	130	3.4	8		NOS	20	Y	N	N		3	1.4	2.6	1.7			NO						0.9	
113	RAJIVGANDHI	23	M	5.7	0.9	140	90	12	296	3.5	19	6	PERIHILAR	10	Y	N	N	UTI	2.9	1.2	3	1.2	3	1.3	NO						1	
114	PADMANABAN	45	M	8	1.2	140	90	9.5	220	3.7	5		NOS	10	N	2+	N		1.6	1.1	1.5	1.2	1.2	1.2	6						1	
115	MUTHUANAND	22	M	5.7	0.9	150	100	13	210	3.5	14		NOS	0	N	N	N		2.4	1.1	2.3	1.1	2.1	1.2	NO						1	
116	AMIRTHAVALLI	24	M	8	1.1	120	80	12.5	120	4	8		NOS	0	N	N	N		2	1	1.5	1	1.2	1.1	5						1	
117	RAJAM	40	F	4.4	0.9	130	90	12.8	128	3.6	16		NOS	20	N	N	N		3.2	1	3	1	2.8	1.1	NO						1.2	
118	AMUDHA	26	F	5.4	0.9	110	70	11	176	3.9	5	1	NOS	10	N	2+	3+		4	1	3	1	2.5	1.1	NO						1.1	
119	MUNUSAMY	60	M	1.8	5	140	80	11	120	3.7	4	1	TIP	40	Y	N	2+		2	4	2.4	4.1	2	4.2	NO				4		3.3	3
120	RAVI	37	M	8.9	0.8	130	80	11.5	289	3.5	24		NOS	10	Y	1+	1+		3	1												
121	ABINASH	16	M	3.2	0.7	130	90	13.8	140	3.2	10		NOS	20	Y	1+	N		2.5	1	2.2	1	2.1	1	NO						2.6	
122	NARASIMMAN	18	M	3.6	0.6	120	90	11	300	4	9		NOS	10	N	N	N		2.5	1	2.2	1.2	2.2	1.2	NO				1.4		5.5	
123	SATHISHKUMAR	15	M	5.3	0.9	110	70	14.2	547	3.8	12		CELLULAR	0	N	2+	3+		3	1												
124	JAYAPAUL	43	M	2.33	7	130	70	12.8	156	3.2	29		PERIHILAR	10	N	N	2+		1.6	4	0.07	1	0.12	1	2	5			1		5.5	
125	LALITHA	20	F	3.7	0.9	120	70	8.5	190	3.2	7		PERIHILAR	10	N	N	N		2.2	1.1	2.1	1.2	2.2	1.2							2.5	
126	SYED KAFIL	47	M	3.9	0.9	150	90	13	120	4.1	7		NOS	10	N	N	N		2.9	1.1	3	1.3	3.1	1.9	NO						2.5	2.5
127	CHELLATHAI	27	F	4.3	1.6	120	80	10	395	3.7	14	2	NOS	10	Y	1+	2+		4.3	1	3	1.1	2.3	1.2							2.5	
128	SEENIVASAN	35	M	5.2	1	120	80	15	120	3.4	15		PERIHILAR	20	Y	2+	2+		3.4	1	3	1.2	2.8	1.3	NO						2.5	
129	AYYAPAN	18	M	4.1	1	130	80	12	295	3.3	14		CELLULAR	20	Y	N	N		3	1												
130	MUNEESWARAN	16	M	6.2	1.3	120	80	13.8	120	3	14	11	COLLAPSE	60	Y	N	N	CUSHING,	6.2	1.4	4				NO						0.8	0.9
131	RAJI	50	M	3.8	0.8	130	80	10.8	200	3.1	10	1	TIP	20	Y	1+	N		1	1	0.2	1	0.12	1.1	2	4			1.2		1.2	
132	SEKAR	32	M	4	1	140	90	12	126	4	7		TIP	50	Y	1+	1+	CUSHING	3.5	1.1	3.5	1.1	3	1.3	NO				1.4		1.5	
133	VIJAYANAND	21	M	2.6	1.1	110	70	13.5	144	3.8	2		PERIHILAR	15	Y	3+	3+	CUSHING	3	1.2	1	1.1	1	1.3	6				1.4		1.4	
134	RAVI	19	M	3.4	1.3	120	80	14	146	4	42		CELLULAR	20	Y	N	N		3	1.2	3	1.3	2.8	1.3	NO				1.8		2	
135	ALAMELU	35	F	4.1	1.3	130	80	12	168	3.8	15		TIP	20	N	3+	3+		2.5	1.1	2.2	1.2	2.2	1.3	NO				1.5		1.5	
136	BALASUBRAMANI	21	M	4	1.5	150	90	11	170	3.4	14		COLLAPSE	30	Y	N	N		3	1.5	2.7	1.5	2.2	1.9	NO				7		6	2.5
137	VIVEKANANDAN	35	M	2.4	1.3	160	100	11	166	3.8	3		TIP	20	N	1+	N		1	1.2	0.1	1.1	0.12	1.1	2	4			1.2		1.2	
138	MOHAMMED HUSS	31	M	4	2	160	100	9	190	3.2	8		NOS	40	Y	N	N		3	2	2.9	2.3	2.5	3	NO						2.9	2.5
139	SUNDARI	45	F	5.8	1.2	140	90	12	210	3	8		TIP	20	Y	1+	N	GLYCEMIA	0.21	1	0.07	1.2	0.2	1.2	1.5	3			1.3		1.3	
140	VENUGOPAL	18	M	2.9	1.4	120	80	11	200	3	7	1	TIP	20	Y	2+	3+	CUSHING	2.8	1.7	2.5	1.5	2.3	1.2	NO				1.3		1.3	

141	MALA	37	F	4.6	1.3	120	80	10.2	270	3.2	4		TIP	10	Y	1+	N		0.2	1	0.12	0.9	0.12	0.9	1	2	2	1,2	1.2		1.3	
142	BHUVANESHWARI	31	F	4.6	1	120	80	13.5	130	4	8		NOS	0	N	N	N	SEPSIS	3.2	1	3	1	2.9	0.1	NO						1.1	
143	SHANMUGAM	60	M	5	3	150	80	12	140	3.3	22		NOS	50	Y	1+	2+		3	3	2.8	3.1	2.7	3.3	NO						4	
144	MANIKANDAN	24	M	5	1.1	110	70	12	380	4.6	15		NOS	10	N	1+	1+			0.8												
145	USHA	30	F	3.4	0.8	150	100	10	230	4.1	9		NOS	30	Y	N	N			0.8												
146	ELAKIYA	22	F	3.2	0.9	180	110	11	220	3.4	23		NOS	15	N	N	N			0.8												
147	VIJAYAKUMAR	17	M	4.2	1.3	110	70	10	150	3	9		NOS	40	Y	N	N		1	1.3	0.2	1.3	0.2	1.4	2	5			3		5	4
148	DINESH	20	M	3.9	1.2	130	80	13	150	3.8	9		TIP	20	Y	3+	2+		3	1.3	2.8	1.4	3	1.8	NO				3.1		7	5
149	SELVARAJ	22	M	4	2.1	110	80	10.5	170	3.4	6		TIP	0	N	1+	1+		1	1	0.2	0.9	0.2	0.9	2	5	1	4	0.8		1	
150	MURALI	14	M	3.5	1.3	130	80	8	120	3	13	5	NOS	40	Y	1+	1+	SEPSIS	3	1.4	2.9	1.5	2.9	1.7	NO				7		7	
151	DHAMU	42	M	6.3	1.9	130	80	12	130	3	6		NOS	20	Y	1+	1+		2.5	1.4	2.4	1.6	2.5	2.4	NO				6		7	
152	KUMAR	16	M	2.7	0.8	100	70	13.2	180	3.4	6		NOS	20	N	N	N		0.2	0.8	0.12	1	0.1	1	1	2			0.9		1	
153	LAKSHMI	24	F	6.4	0.9	130	80	11.5	360	3	12		TIP	30	Y	3+	3+		2.5	1	2.9	1	2.5	1	NO				1.1		1.1	
154	AMSA	40	F	3.9	1.4	90	60	13	240	3.2	5		NOS	10	Y	1+	N		0.2	1	0.12	1	0.2	1	1	2	2	2,3	1.2		1.2	
155	SHAHUL HAMEED	45	M	5.6	1.8	150	90	12	180	3.4	3		NOS	20	Y	N	N		3	2	2.9	2.1	2.5	3	NO				9		7	
156	SATHYARAJ	16	M	5.2	0.8	110	70	14	240	4	7		NOS	20	Y	2+	3+		0.2	0.8	0.12	0.8	0.12	0.9	1	2			0.9		0.9	
157	BHUVANESHWARI	21	F	4.8	0.8	110	70	10.8	200	3.4	9	4	NOS	30	Y	N	N	HEMETEM	3	1	3	1	2.5	1	NO				1.3		1.3	
158	FOWRIA BEGAM	20	F	3.7	2	110	80	9.8	180	3.5	19		CELLULAR	45	Y	N	N		2.5	2.1	2.6	2.3	2.2	3	NO				4.5		7	3.8
159	POWN	40	F	6.6	1.3	150	100	10.8	140	4.5	3		TIP	0	Y	2+	2+		0.2	0.8	0.12	0.9	0.12	0.9	1	3			1		1	
160	KARTHIKEYAN	14	M	2	0.9	100	70	12.8	180	3.8	5		TIP	10	Y	N	N		0.12	0.9	0.12	0.9	0.2	1	1	3			1		1	
161	VIJAY	26	M	7.3	1.8	130	80	12.8	447	3	4		NOS	40	Y	N	N		2.1	2	1.5	2.1	1	2	4				3		3	
162	TOUFIQ AHAMED	17	M	7	0.8	130	80	12	438	3	8		NOS	0	Y	1+	1+		2.5	1	2.2	1.2	2.2	1.3	NO				1.4		1.5	
163	RATHINAM	47	F	5.4	0.8	110	80	9	160	3.7	7		NOS	0	N	N	N		2.5	0.8	2.2	0.9	2.3	0.8	NO						1	
164	RAJESHWARI	27	F	3.7	0.8	150	90	12	210	3	17		NOS	20	N	1+	N		2.3	0.8	2.2	0.9	2.2	0.9	NO						1.2	
165	USHA	16	F	5.1	0.9	110	70	14	200	3.2	4		TIP	20	Y	N	N		2	1	0.2	0.9	0.12	0.9	2	4					1	
166	ELUMALAI	40	M	5.9	1.5	150	90	15	150	3	13		TIP	20	Y	N	N		1	1.3	0.12	1	0.1	0.9	2	4					1	
167	SUSEELA	26	F	2.7	0.8	150	90	13.5	140	3.2	16		TIP	0	Y	2+	N		1.5	1	1	0.9	1	0.9	4				1.2		1.4	
168	SAKTHIVEL	20	M	5.5	1.4	140	90	10.4	498	3.8	12		NOS	40	Y	N	N	ABD TB	3	1.2	2.8	1.4	12.9	2	NO						2.2	
169	KUMAR	29	M	4	1	140	90	11.8	200	2.3	4		NOS	30	Y	N	N		2	1.1	1.2	1	1	1.1	5						1.1	
170	KUBENDRAN	27	M	4.3	1.2	120	70	13.9	230	3.2	12		NOS	0	N	N	N		2.4	1												

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Epidemiological profile ,clinico-pathological correlation and treatment response in adult patients with primary focal segmental glomerulosclerosis INTRODUCTION Focal segmental glomerulosclerosis (FSGS) is a common cause of nephrotic syndrome, accounting for 10% to 35% of nephrotic syndrome in adults. Focal segmental glomerulosclerosis is a pattern of injury defined by a segmental scar, that involves some but not all glomeruli.The prognosis of FSGS in untreated is bad , with 50% patients reach end-stage renal disease (ESRD) at eight years.FSGS account for 20% of dialysis patients and is a common cause of ESRD. The incidence of FSGS has been increasing in recent years. Kitiyakara et al....

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